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STONE IN THE URINARY TRACT IN CHILDREN

A CRITICAL STUDY OF TWENTY-ONE CASES

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CHICAGO

That the incidence of stone in the urinary tract varies in different parts of the world and that there is a variation in the number of cases found in each country are well known facts. One may say, as a general proposition, that the occurrence of stone is relatively rare in the United States, although it is more frequent in some parts of the country than in others.

Stone in the urinary tract in infancy and childhood is a relatively uncommon disease in this country. The literature dealing with it is accordingly limited and made up for the most part of reports of individual cases and of reviews of a large number of cases previously reported. It may therefore be of interest if I describe my personal experiences with the condition.

This paper is based on a study of twenty-one children under 13 years of age. Because of the multiple locations of stone in five of the children, the total number of lesions was twenty-seven.

AGE

The age incidence was from 1 to 12 years, inclusive. The youngest patient had a stone in the bladder; the oldest, stones in the kidney. Of the seven patients who had stones in the bladder but not elsewhere, the youngest was 1 year old and the oldest 11; four were 4 years old or younger, and three were from 9 to 11 years, inclusive. The youngest patient with stone only in the kidney was 8 years old; the remaining five, 10 years or over. The three patients with stone only in the ureter were over 8 years. Of the five patients with stone in more than one organ, one was 2 years and the other three were 10 years old. The age incidence is given in the accompanying table.

From the Children's Memorial Hospital and the Presbyterian Hospital.

Read before the Western Surgical Association, Rochester, Minn., Dec. 6, 1935.

SEX

The general opinion seems to be that in adults there is a marked predisposition to formation of stone in males. That this is also true of children may be seen by the report of Thomas and Tanner,[1] who in their extensive tabulation of cases of stone in the urinary tract in children found one hundred and fifty-five instances in boys and forty-five in girls, a ratio of about 3 to 1. In my series of cases fifteen patients were boys and six girls, which also is a ratio of about 3 to 1.

A review of my cases according to sex shows that of the six patients with stone in the kidney three were boys and three were girls; of the three patients with stone in the ureter, one was a boy and the other two were girls, and of the seven patients with stone in the bladder, all but one were boys. Of the five patients with stone in more than one organ, all were boys.

Age Incidence

Stone in the Kidney	Stone in the Ureter	Stone in the Bladder
8 years.....1 case	8 years.....2 cases	1 year.....2 cases
10 years.....3 cases	11 years.....1 case	4 years.....2 cases
12 years.....2 cases		9 years.....2 cases
		11 years.....1 case
Stone in the Kidney, the Ureter and the Bladder	**Stone in the Kidney and the Ureter**	**Stone in the Kidney and the Bladder**
2 years.....1 case	10 years.....2 cases	9 years.....1 case
		10 years.....1 case

As may be seen by the foregoing analysis, there was only one case of stone in the bladder in a girl. Because of the rare occurrence of this condition in females, especially in children, I am reporting that case:

CASE 1.—*Multiple stones in the bladder in a girl aged 11 years.*

History.—E. M. L., a girl aged 11 years, entered the Children's Memorial Hospital on July 9, 1931. The family history was negative as to stone in the urinary tract. Previous illnesses of the patient were measles, whooping cough, chickenpox and mumps. Incontinence during the day began about four weeks before the patient's admission to the hospital (wetting of the bed had occurred nightly since infancy). At the same time the mother noted the presence of blood in the urine, the quantity of which was small. After a few days the urine seemed to be entirely blood. The hematuria was so profuse that the mother thought it was due to the onset of menstruation. Bearing-down pains in the area of the bladder were present both during and after urination for four weeks. The pain was very severe, and occasionally there were attacks of pain during which no urine

1. Thomas, Gilbert J., and Tanner, Chester O.: Urinary Lithiasis in Children, Minnesota Med. **5**:147 (March) 1922.

was passed. For three weeks prior to her admission the patient had frequency of urination at night as well as in the daytime.

Examination.—Physical examination revealed nothing relevant except slight cervical adenopathy and suprapubic rigidity or tenderness. Examination of the urine revealed an alkaline reaction; specific gravity, 1.012; albumin (4+); red blood cells, white blood cells and an occasional cast. On culture Streptococcus viridans, Streptococcus haemolyticus, colon bacilli and Staphylococcus aureus were found. Inoculation of guinea-pigs gave negative results. Examination of the blood showed red blood cells, 6,710,000, and white blood cells, 13,300, per cubic millimeter; hemoglobin, 80 per cent; nonprotein nitrogen, 28.8 mg., and uric acid, 3.4 mg., per hundred cubic centimeters. A roentgenogram showed the presence of

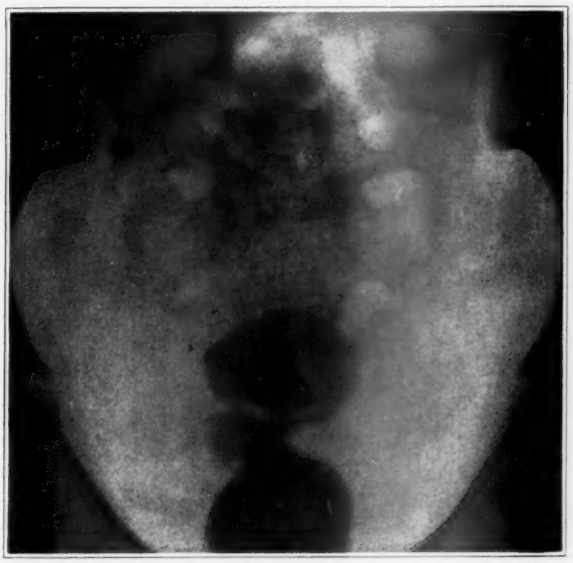

Fig. 1 (case 1).—Multiple stones in the bladder of a girl aged 11 years.

multiple stones in the urinary bladder (fig. 1). An intravenous pyelogram made on July 13 showed the pelvis of the kidneys and the ureters to be normal.

Operation.—A suprapubic cystostomy was performed on July 16. Four large stones and one small stone were removed from the bladder (fig. 2). The bladder was drained with a large, mushroom-shaped catheter. The patient made an uneventful recovery and was discharged on August 25. Chemical examination of the stones showed them to be mainly magnesium ammonium phosphate, with some calcium carbonate and calcium oxalate.

LOCATION OF THE STONES

One of the interesting facts revealed in a study of my cases is that in five of the twenty-one, that is, in 22.8 per cent, stone was present in more than one organ. This is probably a much higher percentage of

multiple locations of stone than one sees in the adult. The distribution of stone in this series according to the number of patients was as follows:

	No. of Patients
Stone in the kidney	6
Stone in the ureter	3
Stone in the bladder	7
Stone in the kidney and the ureter	2
Stone in the kidney and the bladder	2
Stone in the kidney, the ureter and the bladder	1
Total	21

If, however, the series is analyzed from the standpoint not of the number of patients but of the number of times that stone was found

Fig. 2 (case 1).—Four large stones and one small stone removed from the bladder of a girl aged 11 years.

in the various urinary organs, a different set of figures is obtained. There were eleven instances of stone in the kidney, ten of stone in the bladder and six of stone in the ureter—a total of twenty-seven instances of stone in twenty-one patients.

It is to be noted that in sixteen cases stone was present in one organ, whereas in five it was present in more than one. Two patients suffered from a multiplicity of stones both as to location and as to number. One had a stone in the pelvis of the right kidney, a stone in the right ureter and two stones in the bladder (case 2); the other, multiple stones in the left kidney and two stones in the right ureter. The third patient with stone in more than one organ had a stone in the left kidney and

another in the bladder; the fourth, a single stone in the right kidney and a single stone in the left ureter, and the fifth, a stone in the kidney and one in the bladder.

NUMBER OF STONES

Twelve patients had but one stone, while nine had multiple stones. Considering the number of stones, from the point of view of the organ involved, one finds that of the eleven kidneys containing stone, eight contained multiple stones, and three, a single stone. In five of the six instances of stone in the ureter the stone was single, and in one, multiple. In six of the ten instances of stone in the bladder the stone was single, and in four, multiple.

In five of the eleven instances of renal stone, the stone occurred on the right side; in five cases it occurred on the left side, and in one case the condition was bilateral. In three of the six instances of stone in the ureter the stone occurred on the right side and in three on the left.

Three patients had stone both in the kidney and in the ureter. Stone was present in the right kidney and the left ureter of one patient and in the left kidney and the right ureter of another, and in the third patient, who also had stone in the bladder, stone was present in the right kidney and the right ureter.

ASSOCIATED PATHOLOGIC CONDITIONS

In the cases of stone in the kidney and stone in the ureter in which pyelograms were made by the retrograde or intravenous method, evidence of either hydronephrosis or hydro-ureter, or of both, was found. The dilatation that was present at the time of the examination disappeared rapidly after the surgical removal or the spontaneous passage of the stone. The rapidity with which the marked dilatation disappeared was particularly striking in the case of the boy who had a large stone in the right ureter (figs. 3 and 4).

Among the associated pathologic conditions found at the time of operation were an aberrant artery in one case of stone in the kidney, a stone in the bladder in a large diverticulum, obstruction of the neck of the bladder in two cases and a congenital valve in the posterior urethra in one instance.

RETROGRADE MOVEMENT OF STONE

In a previous publication [2] I called attention to the fact that all patients who are to be operated on for stone in the ureter should have a roentgenogram made just before operation to avoid the possibility of the surgeon's operating for ureteral stone only to find that the stone

2. Kretschmer, H. L.: Retrograde Movement of Ureteral Calculi, J. A. M. A. **71**:1355 (Oct. 26) 1918.

has wandered up the ureter or even back into the kidney. I have since observed a retrograde movement of ureteral stone in several patients other than those mentioned in the paper, but I had not observed it in a child until recently, when it occurred in one of the patients at the Chil-

Fig. 3.—An intravenous pyelogram showing enormous dilatation of the right kidney and ureter due to a large stone in the ureter just above the brim of the pelvis.

dren's Memorial Hospital. This patient has previously been referred to in this paper, in the discussion of the occurrence of stone in three locations, that is, in the kidney, the ureter and the bladder. The following report of the case illustrates the retrograde movement of stone:

CASE 2—*Multiple cystine stones, showing retrograde movement of stone in the ureter.*

History.—A. L., a boy aged 2 years, entered the Children's Memorial Hospital on April 29, 1935. Examination of other members of the family brought out the

Fig. 4.—An intravenous pyelogram made six weeks after the removal of the stone shown in figure 3.

fact that the mother had cystine crystals in the urine and that a qualitative test for cystine in the father's urine was positive. The patient was admitted to the hospital with a history of urinary dribbling and straining and severe pain on urination. The dribbling of urine had been present for six months. The pain on

urination was more marked at night. The straining in order to void was often associated with an involuntary movement of the bowels.

Examination.—Physical examination gave essentially negative results. Examination of the urine showed the presence of albumin, blood, pus, red blood cells and cystine crystals (3+). Examination of the blood showed red cells, 4,750,000, and white cells, 8,050, per cubic millimeter; hemoglobin, 90 per cent, and nonprotein nitrogen, 29.2 mg. per hundred cubic centimeters. A phenolsulfonphthalein test showed an output of 92 per cent of the dye in two hours. A roentgenogram made April 17, 1935, had shown the presence of two stones in the bladder, a stone in the pelvis of the right kidney and a stone in the pelvic portion of the right ureter (fig. 5).

An intravenous pyelogram made on April 30 showed moderate hydronephrosis and hydro-ureter on the right side; the left side was normal.

Operation.—A suprapubic cystostomy was performed on July 14, with removal of the stones from the bladder. The patient was discharged on September 5, to return at a subsequent date for removal of the stone from the kidney and the ureter.

Readmission (Oct. 21, 1935).—A roentgenogram made on October 23 showed that the stone which had been located in the pelvic portion of the right ureter was now at the level of the fifth lumbar vertebra (fig. 6*A*). An intravenous pyelogram made on October 23 showed an increase in the hydronephrosis and the hydro-ureter. A plain roentgenogram made on October 31 showed the presence of two stones in the pelvis of the right kidney, the stone previously demonstrated in the lumbar region of the ureter having wandered up into the pelvis (fig. 6*B*). A pyelotomy was performed on the right side on October 31, with the removal of two stones. The kidney was drained through the lower pole and the incision closed with catgut. The patient was discharged on November 11, after an uneventful convalescence. Chemical examination of the stones showed that they were pure cystine.

SYMPTOMS

It is needless to emphasize the importance of early diagnosis of stone in the urinary tract in a child, as well as in an adult, in order to avoid obstruction, with back pressure and damage to the kidney.

As a general rule, symptoms in the child differ little from those in the adult, and they naturally vary, depending on the location of the stone. The great difficulty in making a diagnosis in a child is the probability of a faulty interpretation of the symptoms. Pain, nausea and vomiting are often ascribed to an intestinal upset, and in cases of vesical calculus with imperative urination the condition is often incorrectly diagnosed as enuresis. Furthermore, the condition is often overlooked owing to the difficulty in obtaining a history either because of the age of the child or because the mother or the nursemaid was not observant.

One of the cases illustrates in a striking manner the importance of obtaining a careful history and the value of analyzing the symptoms. The patient, aged 8 years, had two distinct groups of symptoms. It

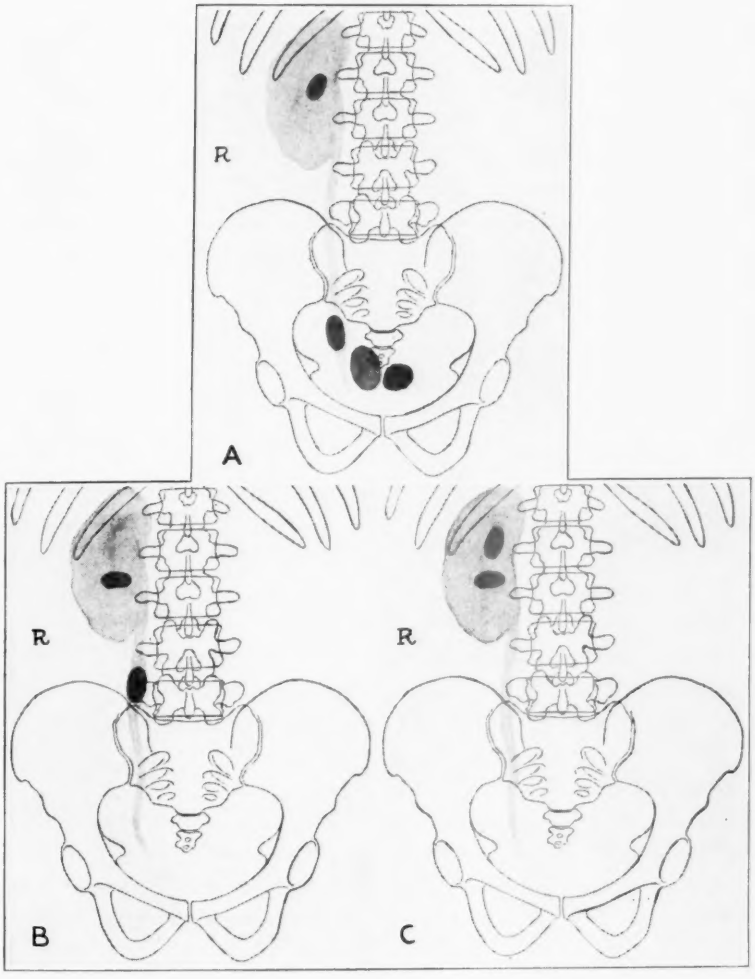

Fig. 5 (case 2).—*A*, roentgen examination made on April 17, 1935, showed the presence of two stones in the bladder, a stone in the pelvis of the right kidney and a stone in the pelvic portion of the right ureter. *B*, roentgen examination made on Oct. 23, 1935, showed a retrograde movement of the ureteral stone from the pelvic to the lumbar portion of the ureter. *C*, roentgen examination made on October 31 showed a further retrograde movement of the stone, from the lumbar portion of the ureter to the pelvis of the kidney.

was stated that she had had enuresis all her life and that three months before she was admitted to the hospital she had passed bloody urine and complained of frequency and difficulty of urination, with accompanying pain and burning. With the onset of this new group of symptoms, it was evident that the condition was not merely enuresis. Complete urologic study showed a stone in the lower part of the ureter, which was subsequently passed.

Onset of Symptoms.—The time between the onset of the first symptom and the date when the patient came under observation showed a variation of from two days in one case to seven years in another. When symptoms were present for more than a year they were of such a character as to suggest that the patient was suffering from organic disease somewhere in the urinary tract.

The period that elapsed between the onset of the symptoms and the examination is given in the following tabulation:

	No. of Cases
2 days	1
From 3 weeks to 2 months	6
From 3 months to 7 months	5
From 1 year to 3 years	8
7 years	1

Pain.—Pain was the symptom most frequently present. It was absent in only two cases, namely, in one case of a solitary stone in the ureter and in one of stone in the bladder. In the first instance the patient was examined because of the presence of pus in the urine on routine examination, and in the second instance the patient was referred from the clinic for syphilis because of dribbling.

In the cases of stone in the kidney the pain was generally described as very severe and located in the area of the kidney. In one case it was referred to the umbilicus. In another (case 2), although the patient had stone in both the kidney and the ureter, he was sent to the hospital because of pain in the bladder on urination, which was due to the presence of multiple stones in the bladder. In the cases of ureteral stone, with the exception of one case in which the patient was without pain, the pain was referred to the kidney on the corresponding side. Pain was present in all except one case of stone in the bladder and was described in five cases as being located in the region of the bladder; in five cases pain on urination was mentioned. In the three cases of stone in both the bladder and the kidney the pain was referred to the kidney.

Hematuria.—In children, as well as in adults, the presence of gross blood in the urine is a very important symptom and one that demands a careful examination of the urinary tract. One of the common causes

of hematuria in the adult is stone in the urinary tract, and it is therefore interesting to note that in the series under discussion gross blood was reported as a symptom in ten of the twenty-one cases, or in 50 per cent.

Disturbances of Micturition.—Frequency of urination was encountered in thirteen cases; pain on urination, in nine; difficulty of urination, in nine; incontinence, in six, and burning on urination, in four.

The symptoms were as follows:

	No. of Cases
Pain	19
Frequency of urination	13
Hematuria	10
Fever	9
Pain on urination	9
Difficulty of urination	9
Vomiting	7
Incontinence	6
Headaches	6
Cloudy urine	5
Burning on urination	4

It is interesting to note that in the child, as in the adult, one sees an occasional case in which there are no symptoms indicative of stone in the urinary tract and in which the condition might be diagnosed as "silent stone." For example, one of the patients, a boy of 11 years, had no symptoms to indicate a stone in the ureter. Owing to the fact that his mother had died of nephritis, the father had a routine examination made of the urine of all the children, during the course of which pus was found in the patient's urine. A complete urologic survey showed the presence of a large stone in the left ureter, with complete destruction of the left kidney.

Passage of Stones.—In the adult it is not uncommon to obtain a history of the passage of sand or gravel in the urine, and it is a relatively easy matter for the patient to recover stones which have been passed. This is considerably more difficult in children. Some authors (Beer [3]) are of the opinion that children pass stones more frequently than is generally supposed.

In three cases in the series under discussion there was a history of passing sand or gravel; in two this was the first symptom noted. In the case of a child of 4 years the mother had noted sand in the child's diaper at the age of 1 year; on reporting this significant symptom to her physician, she was told that it had no significance. Stones were passed in three cases and were recovered in two.

3. Beer, Edwin, and Hyman, Abraham: Diseases of the Urinary Tract in Children, New York, Paul B. Hoeber, Inc., 1930.

DIAGNOSIS

Urinalysis.—Careful and repeated examination of the urine, especially in cases of abdominal pain in which the diagnosis is not clear, are of great value and importance. It seems almost superfluous to emphasize this; yet when one sees children with stone in the urinary tract who have been treated during long periods without having an examination of the urine, or patients who have been treated incorrectly because no examination of the urine was made, one feels justified in stressing this simple yet valuable procedure.

In the twenty-one cases in the series under discussion the urinary studies showed at some time the presence of one or more pathologic elements. Red blood cells, pus cells, albumin, bacteria and crystals are valuable links in the chain of evidence in cases of obscure abdominal pain. In the following tabulation is given the number of cases in which albumin, blood, pus cells or red blood cells were found:

	No. of Cases
Pus	19
Albumin	16
Red blood cells	12
Blood	10

In one case not only did the finding of crystals in the urine prevent an emergency appendectomy, but the type of stone was diagnosed by the kind of crystals (cystine) found.[4]

Bacteriology.—Cultures did not always show the presence of infection. The following types of micro-organisms were observed: Str. viridans, Str. haemolyticus, Bacillus coli, Bacillus proteus, Bacillus pyocyaneus, Staph. aureus, Staph. albus and Diplococcus.

Roentgenographic Findings.—In each case a complete roentgen examination of the urinary tract was made, and positive evidence of stone was obtained in all but one (the case of a stone in a diverticulum). It is interesting to note that in each of the five cases of cystine stone the roentgenogram showed the presence of stone, in spite of the fact that a great many authors are of the opinion that cystine stones cannot be demonstrated by roentgen ray.

Renal Colic Due to Stone.—Two cases not included in the series might well be discussed here from the standpoint of the difficulties encountered in the diagnosis. The patients had symptoms compatible with stone, yet stones were neither demonstrated by roentgen examination nor recovered from the urine. There are several possible explana-

4. Kretschmer, H. L.: Resection of the Kidney, Surg., Gynec. & Obst. **60**:984 (May) 1935.

tions: (1) that the symptoms were due to some lesion other than stone; (2) that the patient passed the stone and it was lost and (3) that the stone was not demonstrable by roentgen examination. Because of the patient's history and the results of repeated pyelographic study, it was difficult to come to any conclusion other than that stone was present. The following is a report of one of the two cases:

CASE 3.—*Renal colic due to stone.*

History.—B. H., a boy aged 11 years, entered the Children's Memorial Hospital on April 16, 1934. His previous illnesses were diphtheria, measles and chickenpox. The mother stated that about five weeks before the child's admission he had an attack of severe pain in the region of his right kidney. The pain was rather sharp, did not radiate and lasted a few minutes, causing him to double up and become pale. A short time after this he passed bloody urine. After the first attack he seemed to be perfectly well until ten days before admission, when he had a similar attack of pain. The following morning he again passed bloody urine. He had marked frequency of urination, being obliged to void about once an hour. He had difficulty in holding his urine, so that at times he wet his clothing. There was some burning on urination.

Examination.—Physical examination revealed nothing pertinent except tenderness in the upper right quadrant of the abdomen. Examination of the urine showed no albumin, sugar or casts in the sediment, pus cells, red blood cells and crystals, and no tubercle bacilli. Examination of the blood showed red cells, 3,700,000, and white cells, 7,750, per cubic millimeter; hemoglobin, 78 per cent, and nonprotein nitrogen, 33 mg. per hundred cubic centimeters. A phenolsulfonphthalein test showed an output of 75 per cent of the dye in two hours.

A roentgenogram made on April 16 showed no evidence of stone in the urinary tract. Intravenous pyelograms made on April 24 showed slight hydronephrosis and hydro-ureter. Intravenous pyelograms made on May 3 showed a marked increase in the hydronephrosis and the hydro-ureter on the right side. The outline of the ureter could readily be traced from the pelvis of the kidney into the bony pelvis, where it seemed to come to an abrupt stop. The rapid increase in the hydronephrosis in nine days was very striking. Intravenous pyelograms made on October 5 (the patient's third admission) showed that the hydronephrosis and the hydro-ureter had completely disappeared; the urinary tract, in other words, was normal.

CHEMICAL COMPOSITION OF THE STONES

One of the interesting bits of information gleaned from a chemical examination of the stones was that in five cases they contained cystine, either pure or mixed. It is, or rather has been, generally assumed that cystine stones are rare; it is therefore interesting to have found so large a percentage (23.8) of cystine stone in so small a series of cases. Three of the cases have been previously reported.[5] In each, other members of the family had cystine crystals in the urine, which emphasizes the well known fact that cystine stone and cystinuria have a decided tendency to run in families.

5. Kretschmer, H. L.: Cystinuria and Cystin Stones, J. Urol. **30**:403 (Oct.) 1933; Urol. & Cutan. Rev. **20**:1, 1916.

Fig. 6 (case 3).—Large hydronephrosis and marked hydro-ureter. The dilatation terminates abruptly in the right ureter. The pelvis of the left kidney and the left ureter are normal.

In the following tabulation are given the results of a chemical analysis of the stones (in some cases the stones were not available for analysis):

Stones from the Kidney

1. Cystine
2. Cystine, uric acid
3. Cystine, uric acid, calcium oxalate
4. Uric acid
5. Uric acid, calcium oxalate
6. Calcium oxalate, phosphate ammonium urate
7. Calcium oxalate, magnesium phosphate, calcium phosphate
8. Calcium phosphate, magnesium phosphate

Stones from the Ureter

1. Cystine
2. Calcium oxalate
3. Calcium oxalate, some phosphate

Stones from the Bladder

1. Cystine
2. Cystine
3. Cystine
4. Uric acid, some amorphous urates
5. Calcium oxalate, ammonium urate, some phosphate
6. Magnesium ammonium phosphate, calcium carbonate, calcium oxalate

TREATMENT

Of the twenty-one patients, four did not undergo treatment. Three of these passed stones spontaneously. The fourth was a girl with a large stone in the kidney, for whom surgical intervention was advised but was refused by the parents, who took the child home without treatment.

In five cases stone was removed from the kidney by pyelolithotomy and in one by nephrolithotomy; in two cases resection of the kidney was also carried out. The patients with stone in the ureter were treated by ureterotomy. Five of the patients with stone in the bladder were treated by suprapubic lithotomy, and five, by litholapaxy. There were no deaths and no postoperative complications.

The indications for the treatment of stone are the same in the child as in the adult. If the stones are small enough to pass, if they produce only slight evidence of obstruction or none at all and if infection is mild or absent, medicinal management is justifiable, that is, the administration alternately of urinary antiseptics and alkaline diuretics. The child should be encouraged to drink large quantities of water, milk, lemonade and other liquids. When the stones in the kidney and the ureter are large, so that they produce definite obstruction, or when there is profuse blood, infection or repeated attacks of renal colic, the patient should be operated on.

INSENSIBLE PERSPIRATION IN CHILDREN

I. EXPERIMENTAL PROCEDURE AND THE INFLUENCE OF CERTAIN FACTORS

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That the body constantly loses weight through the skin and respiratory passages in the form of water vapor and gases [1] has long been known. The exact nature of this phenomenon is still a moot question. Investigators differ as to whether it is a matter of physical diffusion [2] or an active physiologic process [3] and as to whether it is partly [4] or entirely [5] dependent on the activity of the sweat glands or occurs independently.[6] All observers, however, agree that this loss of weight, although invisible, intangible and insensible, is weighable.

That the investigation of the so-called perspiratio insensibilis constituted one of the attractive medical problems of ancient days is evidenced by the aphorisms of Hippocrates and Galen.[7]

From the Pediatric Service of Dr. Béla Schick, Mount Sinai Hospital.

1. The amount of gaseous loss is only from 0.5 to 1 per cent of the total insensible loss. In a general discussion of the insensible perspiration, therefore, the gaseous exchange is usually neglected.

2. Hancock, W.; Whitehouse, G. R., and Haldane, J. S.: Proc. Roy. Soc. London, s.B **105**:43, 1929. Krause: Handwörterb. d. Physiol. **2**:131, 1844.

3. Frieboes, W.: Arch. f. Dermat. u. Syph. **140**:467, 1922. Rothman, S., and Schaaf, F., in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1929, vol. 1, pt. 2. Vasti, A.: Am. J. Physiol. **102**:60, 1902.

4. Barratt, J. O. W.: J. Physiol. **21**:192, 1897. Moog, O., and Buchheister, K.: München. med. Wchnschr. **73**:398, 1926.

5. Jurgensen, E.: Deutsches Arch. f. klin. Med. **144**:193, 1924. Cramer, E.: Arch. f. Hyg. **10**:231, 1890. Schwenkenbecher, A., and Spitta, O.: Arch. f. exper. Path. u. Pharmakol. **56**:284, 1907.

6. Loewy, A., and Wechselman, W.: Virchows Arch. f. path. Anat. **206**:79, 1911. Richardson, H. B.: J. Biol. Chem. **67**:397, 1926. Heller, H.: Ergebn. d. inn. Med. u. Kinderh. **36**:633, 1929.

7. Lusk: History of Metabolism, in Barker, L. F.: Endocrinology and Metabolism, New York, D. Appleton & Co., 1922, vol. 3, p. 7.

What was probably the first quantitative measurement of the insensible perspiration was made by Sanctorius,[8] in 1614, by means of a crude balance of his own construction. His influence was felt for the next two centuries, during which time scales of various types were used by many workers. Weyrich[9] has given a comprehensive review of the earlier investigations. The crudity of the methods and the imperfect understanding of processes of oxidation prior to the nineteenth century, however, make these studies significant only from a historical point of view.

A survey of the later studies in the field can be found in the paper of Benedict and Root.[10] These authors reviewed the development of the more sensitive methods of studying the insensible loss of weight. Although we cannot offer here a detailed historical review of the later developments in this field, we must not fail to stress two outstanding contributions. One is the accurate and sensitive balance which was constructed by Lombard in 1906,[11] by means of which the measurement of the insensible perspiration reached a high degree of accuracy. Unfortunately, the difficulty of constructing this balance has made its general use impossible. The other contribution to which we wish to call attention is that made in 1926 by Benedict and his co-worker,[10] whose studies with the calorimeter and the Sauter balance showed the striking correlation that exists between the production of heat and the vaporization of water through the skin and the lungs. These studies, made on adults, paved the way for Levine and his associates[12] to undertake their comprehensive work of a similar nature with infants.

In the past two years, using the Sauter balance and following the pioneer work of Benedict and of Levine, we have extended the inves-

8. Sanctorius: De statica medicina, translated by John Quincy, ed. 2, London, W. & J. Newton, 1720.

9. Weyrich, V.: Die unmerkliche Wasserverdunstung der menschlichen Haut, Leipzig, W. Engelmann, 1862.

10. Benedict, F. G., and Root, H. F.: Insensible Perspiration: Its Relation to Human Physiology and Pathology, Arch. Int. Med. **38**:1 (July) 1926.

11. Lombard, W. P.: A Method of Recording Changes in Body Weight Which Occur Within Short Intervals of Time, J. A. M. A. **47**:1790 (Dec. 1) 1906.

12. Levine, S. Z.; Wilson, J. R., and Kelly, M.: The Insensible Perspiration in Infancy and in Childhood: Its Constancy in Infants Under Standard Conditions, Am. J. Dis. Child. **37**:791 (April) 1929. Levine, S. Z.; Kelly, M., and Wilson, J. R.: The Insensible Perspiration in Infancy and in Childhood: Proposed Basal Standards for Infants, ibid. **39**:917 (May) 1930. Levine, S. Z., and Marples, E.: The Insensible Perspiration in Infancy and in Childhood: Basal Metabolism and Basal Insensible Perspiration of Normal Infant; Statistical Study of Reliability and of Correlation, ibid. **40**:269 (Aug.) 1930. Levine, S. Z., and Wyatt, T. C.: The Insensible Perspiration in Infancy and in Childhood: Basal Measurements in Dehydrated Infants, ibid. **44**:732 (Oct.) 1932.

tigations to include children. Like our predecessors, we found it necessary to make preliminary studies of those factors which might influence the accuracy of our observations, a knowledge of which has enabled us not only to find the most suitable conditions for our experiments but also to evaluate more critically the data collected.

In this preliminary paper we propose to describe our procedure, to discuss the conditions under which we worked, to record the influence on the insensible perspiration of variations in these conditions and to emphasize the importance of certain factors in the interpretation of our results.

APPARATUS

The room in which our experiments were made is 23 feet long and 12 feet wide. It has a door, four windows opening on the street (north, east and west exposures) and one window opening on a small adjoining examining room, infrequently used. The presence of four radiators makes it possible to regulate the temperature.

A Sauter balance no. 520b,[13] with a capacity of 50 Kg. and a sensitivity of 100 mg., was used to measure the insensible perspiration by the method of serial weighings. Benedict found that the Sauter balance invariably had a larger capacity and greater sensitiveness than were claimed by the manufacturer. We have been able to exceed the prescribed capacity of the scale without altering its sensitivity. The scale is firmly screwed to an oak table in such a manner that free movement of the worm-gear is allowed (fig. 1). During the experiment the subject lies on a bed suspended by flexible chromium-plated chains from the right arm of the scale. The bed swings free of the table, and when weighing is not in process it is rendered immovable by means of wooden props. Two beds are used in our studies: a small, woven metal crib, 110 cm. long, 45 cm. wide and 40 cm. deep, for the infants and a larger, aluminum frame, 160 cm. long, 45 cm. wide and 17 cm. deep, for the older children. A mattress of nonhygroscopic material was early found to be necessary. This mattress is made entirely of rubber sponge, covered by rubber sheeting. The bedding consists of two linen sheets (one used as a cover) and two small cotton-filled pillows, one of which is enclosed in a cotton pillow-slip. On cold days a cotton blanket is used instead of one of the sheets. The weight of the smaller bed with bedding is about 12 Kg.; that of the larger, about 20 Kg.

The clothes worn by the subjects during the experimental procedure invariably consisted of a two piece cotton pajama suit (no stockings) for the older children and a cotton shirt and diaper for the infants.

From the left arm of the scale is suspended a large weighing pan on which the counterweights are placed. A small pan is provided on the right arm of the balance in which additional small weights may be placed when necessary. In the past year we have adopted a procedure, suggested by Benedict,[14] which has materially aided us in eliminating irregularities due to variations in the moisture content of the materials used. This consists in suspending on the left arm of the scale

13. This balance has been adequately described by Benedict (Ztschr. f. d. ges. exper. Med. **91**:340, 1933) and by de Rudder (Ztschr. f. Kinderh. **45**:404, 1928).

14. Benedict, F. G.: Personal communication to the authors.

two cotton sheets and a pajama suit similar to those used in the weighing bed, in order to minimize the difference in gain and loss of moisture on the two arms of the balance.

In our earlier experiments, a tycos sling psychrometer was used for registering wet and dry bulb temperatures. More recently, a Tycos Lloyd hygrodeik has been used and found to be equally accurate. The relative humidity was interpolated from the Taylor tables of relative humidity. The room temperature was read from a centigrade thermometer in the neighborhood of the experimental bed.

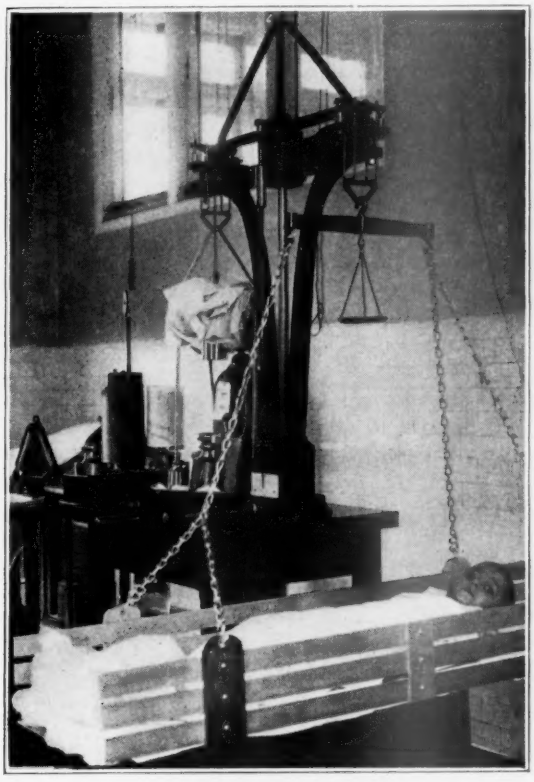

Fig. 1.—The Sauter balance, showing the method of weighings to determine the rate on the insensible perspiration.

EXPERIMENTAL PROCEDURE

Our experiments are regularly carried out in the morning. The subjects are taken from the general pediatric ward and are subjected to the usual hospital routine of bathing and dressing at 6 a. m. A small breakfast is given at 6:30, consisting of 150 cc. of cocoa and one slice of toast. This amount of food and its fluid content are well within the allowance prescribed by Levine and his co-workers in their studies on infants. We found by experiment that such a meal

is without significant stimulating effect either on the basal metabolism or on the basal insensible perspiration two hours after ingestion. As our weighings invariably begin from two and one-half to three hours after this meal, a fasting state is practically achieved. At the same time the discomfort attendant on remaining without food for a prolonged period is avoided. After this breakfast no further food or fluid is given except for purposes of special study. At 9 a. m. the child voids; his temperature is taken, and he is placed in the weighing bed in the pajamas which he has worn since 6 a. m. Care is taken to see that his clothes, hair, face and hands are as dry as possible.

In the weighing bed, in which the bedding has remained overnight, the children seem to be comfortable and either fall asleep or lie quietly during the experimental period—usually from two to three hours, exceptionally as long as five hours. Since only children who are ready to leave the hospital are used in these studies, "being weighed" has come to be looked on as a prerequisite for discharge. This aids us considerably in securing the cooperation of our subjects.

After the child is placed in the weighing bed, counterweights approximating the total weight of subject and bed are placed in the large weighing pan. We have found that the simplest procedure for balancing the scale is to underweigh the subject slightly, as the continuous loss of weight soon effects the balance. Balance is completed when the pendulum swings an equal distance to the two sides of the midline of the dial. The time is then read to the nearest half-minute and recorded. A complete swing of the pendulum is found to consume about thirty seconds. Although the loss of weight is continuous, the amount lost during a complete swing of the pendulum is practically negligible.

Balance having been effected, a 5 Gm. weight is then removed from the weighing pan, and the pendulum is watched for the next moment of balance. This is again recorded, and the same procedure is continued for the duration of the experiment.

During the experiments notes are made as to whether the subject is asleep or awake, quiet or restless (and to what degree), etc. All movements are noted, even during sleep. Without touching the subject, repeated observations are made for the appearance of visible perspiration. When, as occurs only rarely, the trend of the experiment suggests that the subject may be perspiring, palpation is made in the axillae, the small of the back, the soles and the palms. When perspiration is not found observations are resumed. The disturbed period, and sometimes the succeeding one, are excluded from the record. When perspiration is found, the experiment is brought to a close.

At the termination of each experiment the temperature of the subject is again taken, and an examination is made for perspiration.

The room temperature and the relative humidity are recorded at the beginning, the middle and the end of the experiment.

We consider the initial period of our experiments, during which the adjustment of the subject to his environment occurs, an integral part of our observations. The peculiarities of this so-called period of adjustment will subsequently be the subject of a more detailed discussion.

Our computations are made by adding the several individual 5 Gm. periods after basal measurements are obtained and by interpolating this in terms of grams of insensible perspiration lost per hour. We find this method to be more satisfactory than that of obtaining an average from individual 5 Gm. periods, since our observations are continuous and total at least an hour after the initial period of adjustment.

Sources of Error.—In this experimental procedure, errors may arise from:

1. Slight changes in body temperature occurring during the experiment. Niemann [15] pointed out that the slightest rise in body temperature may be responsible for variations in the output of water. His experimental procedure, however, was entirely different from ours, and his observations were continuous over a period of three days. Our experiments lasted for several hours. The temperature of the subject was taken at the beginning and at the end of each experiment. It is therefore unlikely that any significant change in body temperature could have occurred during the experimental period and have remained undetected. Furthermore, the fact that every child was studied for at least two days provided an additional check.

2. The timing of the exact moment of balance of the scale. Since our calculations are based on the time required for the subject to lose 5 Gm., the necessity for observing the exact moment of balance is apparent. Because of the constant movement of the swinging pendulum, the timing of its equidistant swing from the midline of the dial is subject to an error, depending on the vigilance, skill and experience of the observer. This is especially true in our case since we record the moment of balance to the nearest half-minute. However, because of the large number of periods observed over a continuous stretch, we believe that such an error adequately neutralizes itself.

3. The use of clothes and bedding. Authors [16] have called attention to the fact that there is little difference between the insensible perspiration in the nude and that in the clothed state, unless the subject is too cool. The use of such clothes and bedding as are necessary for the comfort of the subject may, however, introduce an error, which must be recognized. We think that this error was not significant in our experiments owing to our use of materials of minimum hygroscopic qualities and, further, because of the adoption of a lengthy period of adjustment which permitted an adequate interchange of moisture between the subject, his clothes and the atmosphere.

4. The computation of results. Our method of recording the insensible loss of weight in grams per hour entails the calculation of an average based on the sum of several short periods of observation. This method introduces a small arithmetical error. We estimated the amount of this error in fifty unselected experiments and found that in no case did any individual period, expressed in grams per hour, deviate by more than 6 per cent (in only one case by more than 5 per cent) from the grams per hour obtained by our method of calculation. We chose this method of calculating the insensible loss of weight because our periods of observation were continuous (not interrupted and selected at random), and the total period usually aggregated at least an hour in addition to the period of adjustment. For purposes of comparison we recalculated our results as averages of individual periods, and here again we found that the deviation from the average for entire observations never exceeded 7 per cent (in all but one case, it did not exceed 5 per cent).

The error usually attributed to variations in the content of feces in the intestinal tract and of urine in the bladder [17] at the beginning and at the end of a period of

15. Niemann, A.: Ergebn. d. inn. Med. u. Kinderh. **11**:63, 1913.

16. Benedict, F. G., and Benedict, C. G.: Skandinav. Arch. f. Physiol. **49**:89, 1926. Meyer, J.: Rev. franç. de pédiat. **1**:409, 1925.

17. Rubner, M., and Heubner, O.: Ztschr. f. Biol. **36**:1, 1898.

observation does not enter the experimental procedure that we have outlined. In our work short period determinations are made on children whose physical needs have been attended to prior to the experiment.

SUBJECTS STUDIED

The children selected for this study were taken from the general pediatric ward. They had come to the hospital for some acute illness and were not studied until from two to four weeks after admission, at which time they were symptom-free and apparently well. More logically, these children should be classified as "hospital normal" since it is conceivable that the prolonged period of hospitalization might, in some way, have affected their metabolic processes. Several of these children have been recalled and restudied since their discharge. A comparison of the results of the more recent studies reveals no significant differences from the findings obtained during hospitalization. The latter observations are as yet too few to warrant abandoning the term "hospital normal."

In all, we studied seventy such children. Individual subjects were observed during from two to twelve experimental days. Although many more experiments were performed, one hundred and sixty-one were finally accepted as satisfactory. Experiments were rejected for any of the following reasons: (1) elevation of body temperature noted at any time during the experiment; (2) the presence of palpable or visible perspiration; (3) extreme variations in environmental temperature or humidity, except as these were being especially studied; (4) manifest restlessness for several periods at the height of the experiment; (5) bedwetting or vomiting (rare), or (6) an insufficient number of periods of observation.

Although numerous additional studies were made on twenty children suffering from a chronic condition, such as diabetes or nephrosis, these have not been used in establishing our standard conditions. The results of these studies and of others in which the effect of certain pharmacologic substances was observed will be the subject of later publications.

The experimental conditions which gave us the most constant results in the group of "hospital normal" children were finally accepted as our standard conditions. The results obtained from these studies will be used in establishing standards of insensible perspiration in children.

The work was carried on from December 1933 to July 1934 and from October 1934 to July 1935. Work had to be abandoned during the summer months, either because the increase in temperature produced visible perspiration, or because the necessary ventilation of the room created conditions which interfered with the accuracy of the results.

We worked with children who could cooperate in making their physical needs known to us, as we wished to avoid the complications introduced by excretory losses through the urine and feces. In the few cases in which voiding was necessary during the experiment, the child was reweighed, and observations were resumed after a suitable period of adjustment.

Using the method described, we have accumulated data on the following factors as they affect the insensible perspiration of children: (1) environmental temperature, (2) relative humidity, (3) activity, (4) sleep, diurnal and nocturnal, (5) food, (6) fluids, (7) clothes and bedding, (8) moving currents of air and (9) psychic and emotional stimuli.

In this paper we shall limit ourselves to a discussion of these data.

EFFECT OF ENVIRONMENTAL TEMPERATURE

Although numerous early observers pointed to an augmenting effect of an increase in temperature on the rate of the insensible perspiration (Erisman,[18] Schierbeck,[19] Janssen[20] and Galeotti and Macri[21]), most of the recent investigations made with the sensitive balance have shown that the effect of environmental temperature within a wide range is slight. Benedict and Root, in a series of experiments in which the room temperature was increased from 16 to 26 C., showed that there was no material alteration in the metabolism or in the insensible perspiration of their male subjects, there being only a slightly greater loss of weight at the highest temperatures than at the lowest. When the skin temperature, however, fell below that normally expected after a night's repose in bed, which happened with their female subjects, the insensible perspiration was decreased. These investigators concluded that within a range of temperature of from 18 to 24 C. variations in the rate of insensible loss of weight are negligible provided the subject is comfortable, neither too cold nor too warm.

Meyer,[22] working with clothed infants, found that there was no effect on the insensible perspiration when the temperature was increased from 18 to 23 C. Levine, who experimented within a range of from 23 to 32 C., found that environmental temperature had no effect on the insensible perspiration unless visible perspiration occurred. He finally adopted a range of from 23 to 25 C. as the zone of comfort for infants.

Our own studies with regard to the suitable range of temperature indicate that if the subject is comfortable, his skin neither unduly cold nor perspiring, the constancy of the insensible loss of weight can be demonstrated within a range of temperature of from 18 to 25 C. (column 4, table 1). Observations on the effect of temperatures above this range showed that such temperatures exerted a profound influence on the insensible loss of weight due to the factor of visible perspiration (subjects 2, 3 and 9, table 1). Conversely, a low room temperature obviously decreasing the skin temperature of the subject below the zone of comfort effected a decrease in the rate of insensible perspiration (subjects 4, 5 and 11, table 1).

18. Erisman, F.: Ztschr. f. Biol. **11**:1, 1875.
19. Schierbeck, H. P.: Arch. f. Hyg. **16**:203, 1893.
20. Janssen: Deutsches Arch. f. klin. Med. **33**:334, 1883.
21. Galeotti, G., and Macri, M. N.: Biochem. Ztschr. **67**:472, 1914.
22. Meyer, J.: Presse méd. **36**:66, 1928.

TABLE 1.—*Effect of Environmental Temperature and Relative Humidity on the Insensible Perspiration*

Column 1	2	3	4	5	6	7	8
Subject	Date	Duration of Experiment, Min.*	Temperature Range, C.	Range in Percentage of Relative Humidity	Insensible Perspiration, Gm. per Hour	Visible Perspiration	Comments
1	6/ 5/34	53	23.5-24	72–74	17.00	Absent	
	6/ 6/34	52	24	86–82	11.50	Absent	
	6/ 7/34	73	20-25	67–72	17.30	Absent	
2	3/30/34	53	21-23	39–41	16.90	Absent	
	3/31/34	72	18-23	55–58	16.67	Absent	
	4/ 2/34	48	26.5-27	40	31.20	Present	
3	11/12/34	43	26-26.5	20	40.00	Present	
	11/27/34	50	23-24	42–45	24.20	Absent	
	12/ 6/34	51	23	50	24.30	Absent	
	12/ 8/34	50	18-20	34	24.00	Absent	
4	2/13/35	38	24-25	9–11	31.00	Absent	
		79	25	11–14	19.00	Absent	
	2/14/35	85	13-17	20	9.50	Absent	
	2/16/35	63	20-21.5	20	14.28	Absent	
	2/20/35	84	20-21	21–24	14.37	Absent	
	2/23/35	62	23	29–37	14.51	Absent	
5	4/16/35	64	15	37	18.75	Absent	Feet cold
	4/19/35	56	21-22.5	44	22.64	Absent	
	4/20/35	49	21	45	23.07	Absent	
6	6/19/34	65	20-23	90	9.00	Absent	
	6/20/34	88	21	82-84	10.00	Absent	
	6/21/34	74	22	80-82	12.00	Absent	
	6/22/34	75	25	69	16.00	Absent	
	6/25/34	55	21	64	16.36	Absent	
	6/26/34	73	22	69	16.43	Absent	
	6/27/34	35	24	75–77	15.00	Absent	
7	6/28/35	82	21	82	10.90	Absent	Predicted loss about
	6/29/35	87	24	83	10.40	Absent	16 Gm. per hour
8	2/ 7/35	81	23	23.5	18.50	Absent	
	2/ 9/35	78	19.5	26	19.10	Absent	
	2/10/35	48	21	19	18.75	Absent	
9	10/15/34	58	18	81	15.50	Absent	
	10/17/34	78	25	48–51	19.40	Absent	
	10/18/34	62	19-20.5	80	14.50	Absent	
	10/19/34	77	23	58–61	19.60	Absent	
	10/30/34	66	26-27	25	30.00	Present	
10	6/13/35	45	24	78–79	13.30	Absent	Predicted loss about
	6/14/35	50	23.5-25	79	13.30	Absent	19 Gm. per hour
	6/15/35	82	23	82	11.10	Absent	
11	11/23/34	81	23	65	18.50	Absent	
	11/28/34	84	21	51–55	17.85	Absent	
	12/ 5/34	85	17	44	14.12	Absent	Feet cold
	12/13/34	46	22	26	16.69	Absent	

* In every case a one hour period of adjustment preceded.

EFFECT OF RELATIVE HUMIDITY

Reports of the effect of the humidity of the surrounding air on the insensible perspiration have been conflicting. One group of investigators held that variations in humidity profoundly affect the rate of elimination of water from this source (Rubner,[23] Vasti, Moog[24] and Erisman); while another group considered that variations in humidity do not appreciably affect the rate of insensible perspiration (Nuttal,[25] Schwenkenbecher,[26] von Willebrand,[27] Eimer,[28] de Rudder, Levine and Benedict).

Our experiments were performed within a range of humidity of from 9 to 90 per cent. Column 6 of table 1 illustrates the variations in the rate of insensible perspiration in eleven selected subjects studied under varying conditions of humidity. It will be noted that within a range of humidity of from 19 to 74 per cent the alterations in insensible perspiration varied well within 10 per cent. Beyond these extremes of humidity, larger variations were observed (subjects 1, 4, 6 and 9, table 1). In the case of subjects 7 and 10 observations were made only on days when the humidity was extremely high. The rate of the insensible loss of weight in these two subjects was definitely less than we expected it to be when compared with the rates on other subjects of similar body build. In cases in which we had an opportunity for comparison of results obtained within a wider range of humidity (subjects 1, 4, 6 and 9, table 1), definite effects were observed attributable to the extremes of humidity. A high humidity (above 74 per cent) was associated with a decrease in the rate of insensible perspiration; a low humidity (less than 19 per cent), with an increase in this rate. Even at the extremes of relative humidity (below 19 per cent and above 74 per cent) the insensible loss of weight was fairly constant, although at different levels.

Changes in the rate of the insensible perspiration outside the accepted range of from 19 to 74 per cent obey the law formulated by Rubner, which states that the elimination of water varies inversely with the humidity.

The ideal condition under which to study the effect of relative humidity on the insensible perspiration would obviously be an environment

23. Rubner, M.: Arch. f. Hyg. **11**:137, 1890.

24. Moog, O.: Deutsches Arch. f. klin. Med. **138**:181, 1922.

25. Nuttal, G. H. F.: Arch. f. Hyg. **23**:184, 1895.

26. Schwenkenbecher, A., in Bethe, A.; von Bergmann, G.; Embden, G., and Ellinger, A.: Handbuch der normalen und pathologischen Physiologie, Berlin, Julius Springer, 1929, vol. 4, p. 709.

27. von Willebrand, E. A.: Skandinav. Arch. f. Physiol. **13**:337, 1902.

28. Eimer, K.: Verhandl. d. deutsch. Gesellsch. f. inn. Med. **41**:519 and 537, 1929.

of constant temperature. Our studies were made within a range of temperature of from 18 to 25 C. However, the work of the majority of observers and our own experiments indicate that variations in temperature within this range are without significant effect. We may therefore accept our observations on the effect of variations in relative humidity within this temperature range to be of distinct significance.

TABLE 2.—*Effect of Activity on the Insensible Perspiration*

Subject	Date	Duration of Experiment, Minutes*	Insensible Perspiration, Gm. per Hour	Comments
1	3/ 5/34	30	27.00	Crying; restless
		51	38.00	Very restless; thrashing about
	3/ 7/34	80	18.75	Quiet; awake
	3/ 8/34	105	18.20	Quiet; awake
2	1/25/34	40	21.80	Sitting up quietly
		60	18.00	Lying down; quiet; awake
	1/26/34	63	18.80	Lying down; quiet; awake
3	3/ 2/34	50	23.25	Moving arms continuously
	3/ 3/34	45	20.00	Quiet
4	3/ 5/35	56	23.00	Crying
		52	17.00	Quiet
	3/ 6/35	71	17.70	Quiet
	3/ 8/35	32	27.69	Talking to self; restless
5	5/ 7/34	106	14.10	Quiet; awake
	5/10/34	76	18.70	Lying quietly but coughing
6	1/25/35	78	26.30	Quiet
	1/29/35	69	26.10	Quiet
	2/ 9/35	70	28.90	Excited about leaving hospital
7	12/24/34	56	16.20	Quiet
	12/26/34	93	16.00	Quiet
	12/27/34	60	20.00	Coughing

* In every case a one hour period of adjustment preceded.

EFFECT OF ACTIVITY

Since Rubner found that a crying infant produces much more heat than a quiet one, and since there is known to be such a close relationship between the production of heat and its elimination through the skin and lungs, one would expect that muscular activity would exert a definite influence on the rate of insensible perspiration. This effect varies, naturally, with the degree of activity. Benedict and Root noticed an increase in this rate amounting to 5 Gm. per hour when their subject changed from the lying to the sitting position. Jores [29] found an increase

29. Jores, A.: Ztschr. f. d. ges. exper. Med. **71**:170, 1930; **74**:757, 1930; **77**:734, 1931.

of from 50 per cent to 60 per cent in the insensible perspiration due to walking. In infants, Hecht,[30] Meyer, Levine and de Rudder found a considerable increase in the insensible perspiration (sometimes as much as 100 per cent) as a result of restlessness or crying.

We made no definite attempts to study the effect of activity on the insensible perspiration, but in the course of our experiments we became aware of its significance in numerous instances in which a child was restless or agitated or sat up during an experiment. The resulting increase in the rate of the insensible loss of weight is shown in table 2. In our observations, which lasted for several hours and in which 5 Gm. period determinations were made, the transitory effect of even a slight degree of restlessness was well demonstrated. Furthermore, studies of the same subject on days when restlessness was absent gave results which contrasted sharply with those obtained during periods of even moderate activity. The more serious types of restlessness, such as crying and thrashing about, always completely invalidated our results.

EFFECT OF SLEEP

In analyzing Levine's studies on infants we noted that in two subjects on whom observations were made during sleep and again during periods of quiet wakefulness, a decrease (of 20 per cent in one and of 23 per cent in the other) occurred in the insensible perspiration during sleep. Meyer demonstrated a decrease of 43 per cent in the rate of insensible perspiration in an infant due to sleep. Benedict, in his adult subjects, found a lower rate in the insensible perspiration during quiet sleep than during restless sleep.

Our observations essentially corroborate these findings. Of the seventy children here reported on, thirty-eight were observed during one or more periods of sleep. In the case of these children, we were able to compare the findings obtained during sleep with those obtained during the quiet waking state. Such a comparison showed a decrease of from 3 to 32 per cent in the insensible perspiration due to sleep (table 3). These variations may possibly be explained by the varying degrees of restlessness during sleep. Confirmation of this explanation may be found in Benedict's overnight studies, in which he observed that when the subject slept quietly, the loss of weight was much less than when there was considerable restlessness. Our own nocturnal observations were limited to nine experiments performed on three children. These limited data confirm Benedict's observations.

The marked variations in the rate of insensible perspiration which occur during sleep justify the use of the quiet waking state for the determination of the basal insensible perspiration. In the study of

30. Hecht, A. F.: Ztschr. f. Kinderh. **38**:193, 1924.

the insensible perspiration of infants, however, the sleeping state is acceptable, since the waking state in this age group is almost invariably associated with uncontrollable activity.

EFFECT OF FOOD

Even to the earliest investigators it was clear that the ingestion of food caused an increase in the insensible perspiration. Schwenkenbecher found this increase to be as much as 50 per cent after a heavy meal. Staehelin's [31] results were similar. Benedict and Root found an increase of from 11 per cent to 27 per cent due to the ingestion of food.

TABLE 3.—*Effect of Sleep on the Insensible Perspiration*

Subject	Date	Duration of Experiment, Minutes*	Insensible Perspiration, Gm. per Hour	Percentage of Decrease Due to Sleep	Comments
1	3/13/35	50	25.26		Quiet; awake
	3/15/35	64	25.20		Quiet; awake
	3/16/35	65	25.43		Quiet; awake
	3/17/35	102	20.00		Asleep; very quiet
	3/18/35	214	17.00	25–32	Asleep; no movements noted
	3/19/35	105	20.00		Quietly sleeping
2	3/ 5/35	75	16.67		Asleep
	3/ 7/35	71	18.72	10–13	Awake; quiet
	3/ 8/35	78	19.20		Awake; quiet
3	2/19/35	63	19.00		Awake; quiet
	2/20/35	54	17.10		Asleep
	3/12/35	59	20.50	10–11	Awake; quiet
	3/14/35	87	17.00		Asleep
4	3/21/35	50	24.74		Awake; quiet
		53	20.70	12–16	Asleep
	3/22/35	56	21.40		Asleep
		62	24.39		Awake; quiet
5	3/14/34	53	17.30		Awake; quiet
	3/15/34	89	16.75	3	Asleep
6	3/10/34	61	19.60		Asleep
	3/12/34	60	20.68	5	Awake; quiet

* In every case a one hour period of adjustment preceded.

Levine, after studying the effect of small meals with varying liquid contents, finally gave his infants meals consisting of a dilution of modified cow's milk low in calories (rarely exceeding 25 calories per kilogram of body weight) and weighing from 20 to 40 Gm. per kilogram. He observed a striking discrepancy between the rate of insensible perspiration during the initial hour after the ingestion of such a meal and that of the succeeding hours, the values for the first hour being notably higher. These observations led him to delay basal measurements of the insensible perspiration for at least one hour after the ingestion of such meals.

31. Staehelin, R.: Ztschr. f. klin. Med. **66**:241, 1908.

Benedict stated that he avoided all possible stimulation of food in his studies by weighing his adult subjects in the starving state. In his experiments, which seldom lasted longer than from one-half to two hours, this regimen was practical.

TABLE 4.—*Effect of the Intake of Food and Fluid on the Insensible Perspiration*

Subject	Date	Duration of Experiment, Min.*	Insensible Perspiration, Gm. per Hour	Basal Metabolism, Total Calories	Food and Fluids Administered†
1	11/ 6/34	55	27.27	1,152	No breakfast
	11/ 7/34	55	27.27	1,159	280 calories, 10% protein
	11/ 9/34	84	28.10	1,117	280 calories, 10% protein, plus 200 cc. of water
2	11/27/34	50	24.20	1,195	280 calories, 10% protein
	12/ 2/34	55	24.40	1,208	No breakfast
3	1/ 4/35	55	27.20	.....	280 calories, 10% protein, plus 150 cc. of water
	1/ 7/35	61	26.80	1,086	No breakfast
	1/ 9/35	44	27.30	1,080	425 calories, 10% protein, plus 300 cc. of water
4	4/ 6/35	75	20.22	.....	400 calories, 10% protein, plus 250 cc. of water
	4/ 9/35	78	20.45	.....	280 calories, 10% protein
5	4/ 2/35	45	21.68	.....	280 calories, 10% protein
	4/15/35	55	21.62	.....	Same as above, plus 500 cc. of water
6	5/ 2/35	50	22.85	.....	280 calories, 10% protein
	5/ 4/35	67	22.64	.....	Same as above, plus 500 cc. of water
	5/18/35	73	22.78	.....	650 calories, 15% protein
7	2/22/35	70	17.02‖		280 calories, 10% protein, 300 cc. of water immediately preceding
		51	17.64§		
	2/23/35	40	16.66	.....	280 calories, 10% protein
		24	12.5 ‡	.....	300 cc. of cold water
		73	16.85§		
8	(Other days)	O'clock	22.0#		
	11/10/34	9-10 a.m.	24.0	.....	350 calories, 27% protein, given at 7:30 a.m.
		10-11	30.0 ¶		
		11-12	26.0		
		12-12:42	21.6		
9	(Other days)	O'clock	21.27#		
	11/ 9/34	9:30-10:30 a.m.	23.0	.....	750 calories, 20% protein, given at 9 a.m.
		10:30-11:30	28.5 ¶		
		11:30-12:30	30.0		

* In every case a one hour period of adjustment preceded.
† All food and fluids were administered from two and one-half to three and one-half hours before the experiment was begun, unless otherwise noted.
‡ Water taken immediately preceding.
§ Subsequent insensible perspiration value after the first twenty-four minutes.
# Usual basal rate of insensible perspiration.
¶ The greatest increase in the rate of insensible perspiration occurred during the third hour.

Our observations were made over periods ranging from two to five hours. We early made preliminary studies which convinced us that the starvation state was not practical for children as it produced a sense of discomfort which tended to increase the rate of insensible loss of weight. We therefore decided to offer a meal which made the child comfortable but which exerted no effect on the insensible perspiration.

In selecting such an experimental breakfast we took into account the total fluid content, the total calories, the specific dynamic action of the food and the time interval between its ingestion and the beginning of the weighings.

Twenty experiments were performed with meals containing varying amounts of fluid and calories. The meals in these experiments, however, were always kept within the limits of 25 calories per kilogram of body weight, and the fluid content never exceeded 25 Gm. per kilogram, except when the effect of fluids per se was being studied—a factor which will later be enlarged on.

The results of these experiments are shown in table 4. Within the range studied there was no essential alteration in the rate of the insensible loss of weight in any subject after a two and one-half hour interval. In two experiments, in which the meal contained an increased amount of protein (20 per cent and 27 per cent) a lingering stimulating effect was noted, which manifested itself most markedly during the third hour after ingestion (subjects 8 and 9, table 4).

We finally decided to adopt a standard breakfast consisting of 150 cc. of sugared cocoa and one slice of toast (280 calories, 10 per cent protein). In the case of the subjects studied this meal never exceeded 23 calories per kilogram for the younger children, while for the older children it amounted to as little as 10 calories per kilogram. The fluid content of this meal was about 14 Gm. per kilogram for the younger children and as little as 5 Gm. per kilogram for the older ones. This standard meal was given at the usual breakfast hour for the hospital (6:30 a. m.). Weighings were begun at 9 a. m. or soon after, thus allowing an interval of at least two and one-half hours.

Comparative studies on three subjects who were given this standard meal and who were also studied in the starvation state revealed no difference in the rate of the insensible loss of weight. Corroborative evidence of this fact was found in their unchanged basal metabolism (subjects 1, 2 and 3, table 4).

The experimental breakfast which we have adopted has been found to be most satisfactory in that it keeps the subjects comfortable and exerts no demonstrable influence on the rate of their insensible perspiration.

EFFECT OF FLUIDS

The effect of varying amounts of fluids administered in single doses has been studied by de Rudder, Dennig,[32] Geréb and Laszlo[33] and Strauss,[34] who stated the belief that the insensible perspiration is entirely

32. Dennig, A.: Ztschr. f. d. ges. phys. Therap. **1**:281, 1898.
33. Geréb, S., and Laszlo, D.: Ztschr. f. klin. Med. **116**:1, 1931.
34. Strauss, H.: Klin. Wchnschr. **1**:1302, 1922.

dependent on the intake of water. Other workers (Levine, Laschtschenko,[35] Moog and Nauck[36] and Atwater and Benedict[37], on the contrary, found that an increase in the intake of fluids leads to an increase in the output of urine without appreciably changing the rate of the loss of water through the insensible perspiration.

In an attempt to decide on the fluid content of our experimental breakfast, we studied the effect of single doses of water varying from 200 to 500 cc. The procedure followed was to give the additional water (at room temperature) either with the regular experimental breakfast at 6:30 a. m. or after the subject had arrived at a constant basal loss in the usual way. Eight observations on six children showed no change in the rate of the insensible perspiration attributable to the fluids given at either time (table 4). In several subjects not listed in the table an increase in the administration of fluids apparently excited a *Wasserstoss* effect which necessitated voiding during the experiment. Even in these cases, however, the rate of insensible loss of weight remained essentially unaltered. In one subject four experiments performed on two successive days showed a decrease in the rate of insensible perspiration after the administration of 300 cc. of cold tap water (subject 7, table 4). This decrease lasted only during the first 5 Gm. period after the administration of the fluid, the rate immediately thereafter returning to normal. The decrease in this case was attributed to the fact that the water was cold and that the heat utilized in raising the water to body temperature was not available for vaporization through the usual channels accounting for the insensible loss of weight.

In spite of the fact, however, that the insensible perspiration remained unaltered by as much as 500 cc. of administered fluids, we nevertheless decided to keep the fluid content of our experimental breakfast as low as 150 cc. We thus averted the interruption of our experiments caused by the necessity for voiding.

EFFECT OF CLOTHES AND BEDDING

Benedict pointed out that in those laboratories in which discrepancies in the insensible perspiration were observed insufficient attention was paid to the materials used in the experiments. He found that the rate of insensible perspiration remained practically the same when the subject was either naked or clothed provided the clothing and bedding used were, as far as possible, nonhygroscopic. Levine and his associates also found that the rate of insensible perspiration in infants was practically

35. Laschtschenko, P.: Arch. f. Hyg. **33**:145, 1898.

36. Moog, O., and Nauck, E. T.: Ztschr. f. d. ges. exper. Med. **25**:385, 1921.

37. Atwater, W. O., and Benedict, F. G.: Experiments on the Metabolism of Matter and Energy in the Human Body, Bulletin 136, U. S. Dept. Agric. Off. Exper. Stat., 1903, p. 95.

independent of clothing which was carefully planned with an eye to nonhygroscopic qualities.

Although it is practically impossible to avoid entirely the use of hygroscopic materials, these should be reduced to a minimum compatible with the comfort of the subject. It is our experience that under such conditions irregularities, seemingly cryptic, will in a large measure disappear. In planning the clothes to be used for our experiments, we decided to use cotton materials only, as far as this was possible. Accordingly, we have adopted a two piece pajama suit for the older children and a shirt and diaper for the infants. The bedding was similarly planned with an eye to reducing hygroscopic materials to a minimum. A rubber sponge mattress, two small cotton-filled pillows, one pillow-slip, one under sheet and one top sheet (the latter replaced in cooler weather by a cotton blanket) constituted our equipment of bedding. We adopted the suggestion of Dr. Benedict that we counterbalance the scale with materials identical with those used in the weighing bed. Using this procedure and the equipment described, we have noted a more rapid stabilization of the rate of insensible loss of weight, as well as smaller variations in our results.

EFFECT OF AN INCREASE IN VENTILATION

There are diverse reports in the literature on the effect of moving currents of air on the rate of insensible perspiration. Erisman found that an increase in ventilation had no effect on the rate of evaporation through dead skin, but he observed a marked increase in the insensible perspiration from his arm when exposed to a current of moving air. Wolpert [38] and Loewy [39] found that ventilation had no effect on the insensible perspiration provided the surrounding temperature was neither too high nor too low. Schwenkenbecher pointed out that moving air had no effect on the rate of insensible perspiration as long as it did not involve a change in the regulation of heat. McClure and Sauer [40] stated the belief that an increase in ventilation increases the rate of the insensible perspiration until a cooling effect prevents further increase. Osborne [41] found that the loss of water and carbon dioxide through the skin and the lungs was definitely increased by cold dry moving air. Benedict and Benedict reported that "the act of disrobing and subjecting the body to a blast of room air from a strong electric fan frequently

38. Wolpert, H.: Arch. f. Hyg. **33**:206, 1898.

39. Loewy, A.: Biochem. Ztschr. **67**:243, 1914.

40. McClure, W. B., and Sauer, L. W.: Observations Regarding the Loss of Water Vapor Through the Skin in Infants, Arch. Int. Med. **21**:428 (March) 1918.

41. Osborne, W. A.: J. Physiol. **41**:345, 1911.

did not alter in the slightest the insensible loss." Wiley and Newburgh,[42] on the contrary, found that a current of moving air created by an electric fan definitely decreased the rate of loss of weight in their nude subjects.

Our studies on the effect on the insensible perspiration of an increase in ventilation were made on subjects in the clothed and in the nude state. The methods used for increasing ventilation were: (1) opening windows to produce a draught by cross-ventilation, and (2) creating a direct continuous current of air by means of an electric fan. The experiments were performed in the usual manner. Under standard conditions the rate of the insensible loss of weight was permitted to become constant. The subject was then exposed to the increased ventilation. A careful record of the room temperature and the humidity was kept throughout the entire experiment.

Our observations were divided into two groups: (1) eight observations made on five clothed subjects and (2) seven observations made on four nude subjects. The results are shown in table 5. The method of securing the increase in ventilation in the individual cases is recorded in column 6, table 5. Since the purpose of these experiments was mainly to establish standard conditions for our studies, no attempt was made to compare the effect of the two methods of increasing ventilation. Such a comparison, however, made in one case (subject 3, table 5) showed no essential difference in the effect on the insensible perspiration.

Of the clothed subjects, four (subjects 1, 2, 3 and 4, table 5) showed a definite increase (of from 14 to 20 per cent) in the rate of insensible perspiration. This increase was independent of the method used for securing the increase in ventilation. In the studies on these subjects the room temperature and the humidity remained essentially unchanged (columns 2 and 3, table 5). In subjects 4 and 5 (table 5) there was a decrease of 21 and 31 per cent, respectively, in the rate of insensible perspiration. In the case of these two subjects, the room temperature during the period of the increase in ventilation dropped from 24 to 15 C. and from 21.5 to 14 C.

In the nude subjects there was a uniform decrease (of from 11 to 21 per cent) in the rate of insensible perspiration during the period of the increase in ventilation produced by either method. In the case of these subjects there was no significant change in the room temperature or in the humidity during this period.

In interpreting these results and those of other workers, two considerations must be borne in mind: (1) the effect of an increase in ventilation on the rate of evaporation of moisture from body to clothes to atmosphere and (2) the degree to which the heat-conserving function of the skin is brought into play. The latter factor is intimately tied up with changes in skin temperature. When an increase in ventilation

42. Wiley, F. H., and Newburgh, L. H.: J. Clin. Investigation **10**:689, 1931.

increases evaporation without the necessity arising for a change in the conservation of heat, the result is an increase in the rate of insensible perspiration (clothed subjects 1, 2, 3 and 4, table 5). On the other hand, when as a result of an increase in ventilation evaporation is increased to a point where cooling of the skin takes place, the mechanism for the conservation of heat is brought into play, and the result is a decrease in the rate of insensible perspiration. This process is illustrated

TABLE 5.—*Effect of an Increase in Ventilation on the Insensible Perspiration*

Column 1		2	3	4	5	6	
Subject	Date	Temperature, C.	Percentage of Relative Humidity	Insensible Perspiration, Gm. per Hour	Percentage of Change in Rate of Insensible Perspiration	Draught Created by*	Comments
				Clothed Subjects			
1	May 29	23.0	50.0	12.76			
		24.0	51.0	15.39	Increase, 20	Open windows	
2	May 23	22.0	38.0	19.35			
		22.5	38.0	23.40	Increase, 14	Electric fan	
3	May 22	24.0	37.0	22.78			
		24.0	37.0	26.55	Increase, 16	Electric fan	
	May 24	22.0	39.0	22.22			
		21.5	36.0	26.45	Increase, 19	Electric fan	
	June 2	23.0	43.0	22.85			
		24.0	39.0	27.20	Increase, 19	Open windows	
4	April 27	24.0	35.5	18.37			
		23.0	35.5	21.80	Increase, 18	Open windows	
	April 2	24.0	68.0	18.46			
		15.0	51.0	14.30	Decrease, 21	Open windows	Note drop in temperature
5	Dec. 15	21.5	29.0	14.50			
		14.0	27.0	10.00	Decrease, 31	Open windows	Note drop in temperature
				Nude Subjects			
1	June 12	25.0	67.0	18.75			
		25.0	67.0	16.67	Decrease, 11	Electric fan	
2	June 4	24.0	66.0	18.18			
		24.0	66.0	14.77	Decrease, 18	Electric fan	
3	June 2	23.0	45.0	18.57			
		23.0	44.0	15.00	Decrease, 19	Open windows	
	June 3	24.0	47.0	18.50			
		24.0	47.0	14.60	Decrease, 21	Electric fan	
	May 31	25.0	53.0	18.19			
		25.0	53.0	15.00	Decrease, 17	Electric fan	
4	June 1	23.0	50.0	12.87			
		24.0	51.0	10.29	Decrease, 20	Electric fan	

* A draught was created only after subject had been brought to the basal rate.

especially in the case of the nude subjects (table 5). In clothed subjects 4 and 5 (table 5) cooling of the skin probably resulted from a drop in the environmental temperature.

A more detailed and more critical study of the effect of an increase in ventilation will shortly be undertaken and will include an analysis of findings in the same subjects under the different experimental conditions, namely, clothed, nude, exposed to draughts created by open windows and electric fans, etc., together with studies of the skin temperature under the varying conditions.

It should be here emphasized that the present studies were made chiefly with an eye to determining whether an increase in the ventilation in the room in which our experiments were conducted would alter our basal results. Because our results were considerably altered, we early decided on a policy of keeping the windows opening on the street closed during all our experiments. We usually opened the inside window, a procedure which made possible a comfortable temperature and adequate ventilation without creating draughts which might have affected our results.

EFFECT OF PSYCHIC AND EMOTIONAL STATES

The importance of securing the comfort of the subject and the necessity of procuring his complete mental and physical relaxation were early recognized by us. Apprehension or displeasure on the part of the subject, especially on the first day of observation, when the experience was novel, frequently expressed itself in a definite prolongation of the period of adjustment or in an increase in the rate of insensible perspiration. In two such cases we were obliged to discard the first day's findings because a comparison with the results on succeeding days demonstrated the importance of the psychic element. In a third case, when the child knew he was to be discharged from the hospital in the afternoon, an increase in the rate of insensible perspiration was found that morning (subject 8, table 2). A comparison of these results with those of preceding days on which the subject had been under no emotional strain again emphasized the importance of the psychic factor. When experiments were unduly prolonged and the factor of fatigue or hunger entered, we noted a more rapid insensible loss even though the subject was apparently quiet. Our routine was planned, as far as possible, with a view to avoiding psychic or emotional stress that might influence our results.

CONSTANCY OF RESULTS

The constancy of results obtained by using the Sauter balance for measuring the loss of weight due to insensible perspiration has been stressed by many observers (Meyer, de Rudder, Benedict, Levine and Baumecker and Schonthal [43]). Our own experience confirms these observations.

The period immediately following the initial weighing of the subject regularly presented findings which contrasted sharply with those obtained later in the experiment. This so-called period of adjustment involves an interchange of moisture between the subject, his clothes, the bedding and the atmosphere, until a state of equilibrium is established.

43. Baumecker, W., and Schonthal, L.: Ztschr. f. Kinderh. **40**:211, 1926.

Considerable variations in the duration of the period of adjustment and irregularities in the rate of loss of weight during this period, have been reported by many authors. Such variations in our own results demanded our attention. We noted that in some children the rate of insensible loss of weight became constant within as short a time as fifteen minutes. In a few the rate did not become constant until an hour had elapsed. The majority of our subjects showed a constant loss of weight within thirty minutes.

Again, most observers have found that the rate of insensible loss of weight during the individual periods of the phase of adjustment is rapid at first and then gradually slows until it assumes a constant basal level. Although this was our usual experience, there were several subjects in whom the rate of loss of weight was lower during the early 5 Gm. periods than during succeeding 5 Gm. periods.

The reasons for such variations are not entirely clear to us. In studying the factors which may be responsible, we investigated the following ones:

1. The temperature of the ward from which the subjects were taken as compared with that of the weighing room. When the former was from 6 to 8 F. higher than the latter, we noticed that the initial 5 Gm. period tended to be prolonged. When the two temperatures approximated each other, the initial period was relatively short. In several cases the ward temperature was lower than that of the weighing room, but the difference was so slight that no change was observed in the length of the initial 5 Gm. period.

2. The activity attendant on the transfer of the subject from the ward to the weighing room. We noticed that in children who resisted transfer, or who were particularly active during preparation for transfer, there was a distinct increase in the length of time required before basal measurements were obtained. As a result of several observations of this kind, we made it a policy to use only cooperative subjects and, further, to carry them into the experimental room instead of allowing them to walk.

3. The activity of the child prior to the experimental period. Although no accurate record could be obtained of the activity of the child between the moment of his awakening and the beginning of the experiment, we noted in isolated instances that such activity when intense prolonged the period of adjustment.

4. The psychic stimulation aroused by the novel experience. On several occasions on which marked apprehension on the part of the subject was apparent, a prolongation of the period of adjustment was noted, especially on the first day of observation.

Any or all of these factors may account for the irregularities which occurred during the period of adjustment. These irregularities caused

the question to be raised whether an arbitrary period should be adopted as the period of adjustment, or whether a variable duration, depending on the time required for stabilization in each case, should be accepted. Most authors have adopted the latter procedure and accepted the rate as basal as soon as it became constant. In view of the fact that our experiments lasted a minimum of two hours and comprised a large number of individual periods, we decided to adopt a uniform period of adjustment of one hour. We realize that we have been overcautious in allowing such a long period. However, this length of time satisfactorily encompassed every case included in our study.

After the period of adjustment, the loss of weight from period to period became practically a straight line function of the time intervals and remained so for hours. This is illustrated in figure 2, which shows a record typical for all the subjects studied. In addition, these subjects

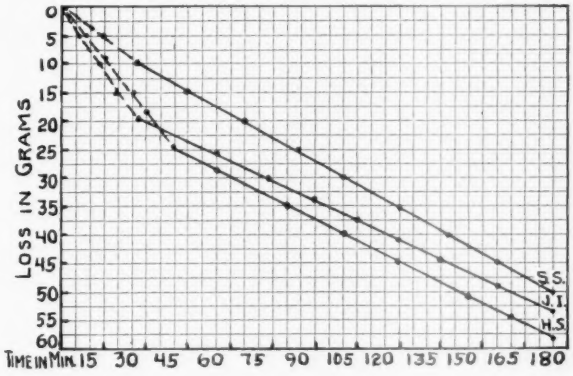

Fig. 2.—An illustration of the constancy of the rate of insensible perspiration under standard conditions.

maintained a constant rate of insensible perspiration from day to day. Under our standard conditions variations in this rate never exceeded 10 per cent. More often they were no greater than 5 per cent, and in many cases, even less.

Since the method of weighings by the Sauter balance gave variations which fell well within the limits of experimental error, we have used it in the study of numerous biometric correlations. The results of these studies will be reported in subsequent papers.

COMMENTS

It is apparent that the variability of results that has freequently been reported in the literature [44] may in a large measure be due to the diverse

44. Lasch, W.: Ztschr. f. Kinderh. **36**:42, 1923. Hirsch, L.: ibid. **41**:653, 1926. Heller, H., and Schwartz, O.: Ztschr. f. d. ges. exper. Med. **73**:481, 1930.

methods employed and the sources of error inherent therein. To evaluate data accurately from a comparative standpoint, one must take into account the similarity of experimental procedure. We have therefore compared our findings with those of Levine and his co-workers and with those of Benedict and his associates. In the light of these comparisons, we can corroborate for the age group between 2 and 14 years the findings previously presented by these authors.

In the course of our experiments, we have come to accept as our standard conditions a range of temperature of from 18 to 25 C. in the absence of visible perspiration and a relative humidity of from 19 to 74 per cent. We use a minimum of hygroscopic materials for clothes and bedding. We attempt to have our subjects thoroughly relaxed physically and mentally. We find it desirable to allow a small breakfast containing not more than 25 calories per kilogram, with a fluid content not exceeding 40 Gm. per kilogram. This breakfast is served at least two and one-half hours before the initial weighing. We have found this meal to be nonstimulating after such an interval.

Under these conditions and with the procedure outlined, we obtain findings in subjects at rest which when tests are repeated from day to day show minimal variations. Results so obtained may be considered basal.

It should be emphasized that our subjects were convalescent children apparently free from disease and ready for discharge from the hospital. The term "hospital normal" has been applied to this type of subject. We wish to point out, however, that several of these children were readmitted for study after their discharge and that no significant variations in the rate of their insensible perspiration were found.

In our experiments, we have chosen to avoid infants, first, because Levine and his associates have adequately covered this field; second, because we have wished to complicate our work with as few factors as possible, and third, because when we undertook this study the literature did not contain findings for the age group with which we proposed to work. We are now able to furnish additional experimental data to substantiate the curve which Levine plotted to indicate the rate of insensible perspiration from infancy to old age. These data will subsequently be published.

SUMMARY AND CONCLUSIONS

The sensitive Sauter balance was used in the study of the insensible loss of weight in seventy children from 2 to 14 years of age. The children were taken from the general pediatric ward of the hospital. They were symptom-free and ready for discharge. These subjects may be termed "hospital normal." In all, one hundred and sixty-one acceptable experiments were performed on this group. Each subject was observed

during from two to twelve experimental days. Each experiment lasted from two to three hours (exceptionally for as long as five hours) and included a minimum of three continuous individual periods of observation, in addition to a one hour period of adjustment.

In this paper we have described our procedure, discussed the conditions under which we worked and the influence on our results of variations in these conditions and compiled and evaluated our results.

The experimental conditions which gave us the most constant results in the group of "hospital normal" children were finally accepted as our standard conditions for measuring the insensible perspiration. These conditions are: (1) the subject awake but thoroughly relaxed physically and mentally; (2) a small meal given at least two and one-half hours preceding the initial weighing, containing 280 calories, with a fluid content of 150 cc.; (3) the clothing and bedding planned with an eye to having a minimum of hygroscopic materials; (4) a range in temperature of from 18 to 25 C., in the absence of visible perspiration, and (5) a range in the relative humidity of from 19 to 74 per cent.

The results obtained under these conditions may be termed basal in the same sense as this term is applied to the basal metabolism. Studies made with the subject asleep gave values ranging from 3 to 32 per cent lower than those obtained during the waking state. These values were not considered basal for the older children since the variations were sufficiently great to constitute an important error. This is in contrast to the requisite sleeping state in the study of the insensible perspiration in infants, in whom the waking state is almost invariably associated with uncontrollable activity.

The possible sources of error under these standard conditions have been discussed. Slight errors may arise from uncontrollable sources inherent in the procedure proper or from the computation of results, which for all practical purposes may be ignored. Larger and more significant errors may necessitate the rejection of an experiment. These may arise from: (1) elevation of body temperature during the experiment; (2) the presence of palpable or visible perspiration; (3) extreme variations in the environmental temperature or the humidity; (4) manifest restlessness during the experiment; (5) bedwetting or vomiting, or (6) an insufficient number of periods of observation.

When care is taken to avoid such errors, the method is accurate. Our studies show a constancy of results, with maximum variations never exceeding 10 per cent.

The method of measuring the insensible perspiration by means of the Sauter balance is now being used by us in the study of numerous biometric correlations, the effect of certain noxious agents and the influence of pathologic states.

SENSITIVITY TO TUBERCULIN AT DIFFERENT AGE PERIODS

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In important respects the specific allergy regularly induced in the tissues by an initial infection with tubercle bacilli is a peculiarly variable immunologic change. The intensity of the reaction to a standard dose of tuberculoprotein varies markedly in infected patients, and, apparently, after attaining a maximum development, the degree of sensitiveness to the material tends in general to diminish slowly as postcontamination years elapse. Furthermore, casual observation has indicated that the size of the average area of reaction to a standard dose of tuberculin is smaller in infected adults than in allergic children.

In order to investigate this last point, careful measurements were made for a series of adults and children of the fields of erythema of the Mantoux reactions to 0.02 mg. of old tuberculin [1] and to 0.0001 mg. of purified protein derivative applied simultaneously in each instance on the right and left forearms, respectively. A modification of Hammar's area-by-weight method, as described elsewhere,[2] was used in this study for determining the areas of the zones of erythema, and readings were recorded for each patient at the end of each of four successive intervals of twenty-four hours following the performance of the Mantoux tests. Measurements were made for a total of 220 infected patients: 120 children attending the Lymanhurst School and 100 adults in the University Hospital. The ages of the children ranged from 8 to 17 years, and the ages of the adults, from 20 to 84 years. In order to obtain observations on a group of 100 tuberculin-sensitive adults, it was necessary to apply Mantoux tests to a total of 197 University Hospital patients, as only 50.8 per cent of these patients gave a positive reaction. This experience indicates that sensitivity to tuberculin is less prevalent among adults in some districts than is generally believed to be the case.

The average sizes of the areas of reaction at the end of each of four successive intervals of twenty-four hours after the administration

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1. Throughout this work the old tuberculin used was that described by Dorset (J. Am. Vet. M. A. **37**:439, 1934).

2. Stewart, C. A.: Cutaneous Reaction to Tuberculin in Primary Pulmonary Tuberculosis: Growth and Variability of Surface Area, Am. J. Dis. Child. **45**: 1229 (June) 1933.

of each material, as well as of the maximum sizes attained by the reactions,[3] are shown in table 1 for different age groups. In general, the areas of reaction to old tuberculin were smaller than those to purified protein derivative, and this difference was noted in children as well as in adults. The two materials used, therefore, were not administered in doses of equal potency. Nevertheless, as will be pointed out later, the situations disclosed by each test material relative to the degree of sensitiveness to tuberculin present in different age groups were in agreement.

According to the data (table 1), the reactions to each test material attained a greater mean size in children than did the responses in either group of adults to the corresponding material, and this difference in favor of the children disclosed by each preparation of tuberculoprotein

TABLE 1.—*The Average Areas of Reactions to 0.02 Mg. of Old Tuberculin and to 0.0001 Mg. of Purified Protein Derivative (Seibert) in Children and in Adults at the End of Each of Four Successive Intervals of Twenty-Four Hours and the Average Maximum Areas of Reaction*

Range of Ages, Years	Number of Patients	Area of Reaction to Old Tuberculin, Sq. Cm. 24 Hours	48 Hours	72 Hours	96 Hours	Area of Reaction to Purified Protein Derivative, Sq. Cm. 24 Hours	48 Hours	72 Hours	96 Hours
8 to 17	120	8.1	6.4	3.2	1.9	14.5	13.2	8.2	3.8
20 to 39	42	3.7	6.5	5.8	2.9	3.3	10.8	10.2	5.2
40 to 84	58	2.6	2.3	1.6	1.2	2.2	5.7	3.1	2.0
All adults	100	3.1	4.1	3.4	1.8	2.6	7.8	6.2	3.3

		Average Area, Sq. Cm.*	Maximum	Percentage of Average Decrease	Average Area, Sq. Cm.*	Maximum	Percentage of Average Decrease
Children	120	9	....	....	22.7	....	.....
Adults	100	..	4.9	45.6	....	8.5	62.6

* Disregarding the time required for the reactions to reach full development.

roughly paralleled the difference in ages. Also, throughout the periods of increment and decline, the Mantoux reactions to each test material were for the most part consistently larger in the children than in the older adults. When a similar comparison is made between the children and the younger adults, the greater mean reaction noted for the former is found not to persist beyond the forty-eighth hour after the tests were made. In addition, averages based on the maximum sizes attained by the reactions[3] also agree with the observations made at the end of four successive twenty-four hour intervals to the effect that children are more allergic than adults. On the whole, therefore, the results obtained for each test material agree in indicating roughly that the average degree of sensitiveness to tuberculin, as expressed in terms of the areas of reaction, is inversely proportional to the age of the patients. These findings are interpreted as evidence that, quantitatively,

3. Disregarding in this instance the time required for each reaction to reach its full development.

allergy in children and that in adults are not strictly identical immunologic states. The differences in sensitiveness to tuberculoprotein noted between patients in different age groups probably is an expression of a general tendency for the responsiveness of allergic tissues to tuberculin to diminish gradually as the postinfection time increases.

Curves representing the changes at twenty-four hour intervals in the average sizes of the reactions to each test material used are shown in figure 1 for the purpose of providing a concise graphic representation of the situation disclosed by the data in table 1. Attention is called merely to the fact that the peaks of the curves of growth in the reaction areas of the younger adults are seen to lie between the crests of the curves for the youngest and oldest groups of patients, respectively.

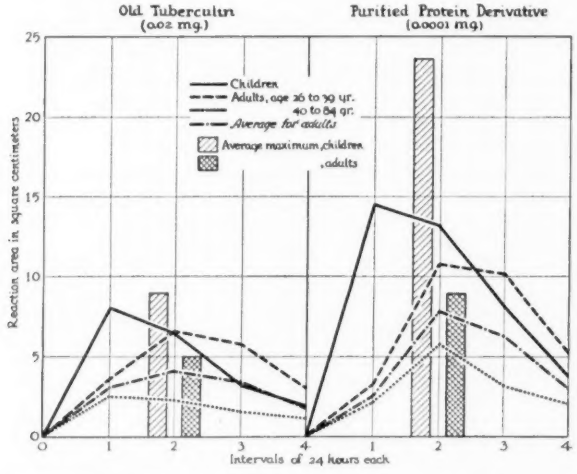

Fig. 1.—Graph showing the growth of the areas of the Mantoux reactions at twenty-four hour intervals.

Since allergy in children seems to differ quantitatively from that in adults, the desirability of attempting to analyze this situation by determining the character of the distribution of various degrees of sensitiveness of the skin in each of these two age groups becomes apparent. In order to test this point the data were arranged in contingency tables (tables 2 and 3) from which the values for chi-square were computed. The compilation of contingency tables suitable for comparing the distribution of different degrees of allergy in these two age groups first involved arranging the readings made for the children and for the adults at the end of the first twenty-four hour period into separate ascending series according to the size attained by the individual reactions, not only to old tuberculin but also to purified protein derivative. The limits within which the individual reactions to each test material varied for each successive more allergic quartile (25 per cent) of the

group of children were then determined, and these quartile area-ranges were used as a standard for comparison. Finally, the numbers of adults with reaction areas at the first twenty-four hour reading that

TABLE 2.—*The Distribution of the Adults, Using the Quartile Range in Areas of Reaction (0.02 Mg. of Old Tuberculin) for Children as a Norm, and the Significance of the Difference Noted (Chi-Square)*

	Number of Adults with Areas Falling Within the Limits Noted for Each Quartile of Children						Chances per Thousand for the Differences to Arise by Accident (P)
	Quartiles					Chi-Square N = 4*	
	1	2	3	4	Total		
	24 Hour Readings						
A. Children, 8 to 17 years	29	29	29	29	116	48.13	0
B. Adults, 20 to 84 years	67	22	8	3	100		
A + B	96	51	37	32	216		
$\frac{\text{A values}}{116}$ (for children)	0.25	0.25	0.25	0.25	1.00		
$\frac{\text{B values}}{100}$ (for adults)	0.67	0.22	0.08	0.03	1.00		
Difference in percentages	−0.42	+0.03	+0.17	+0.22	0.00		
Squared difference	0.1764	0.0009	0.0289	0.0484			
$\frac{\text{Squared difference}}{\text{A + B}}$	0.0018375	0.000017647	0.00078108	0.0015125	0.004218727		
	48 Hour Readings						
A. Children	29	29	29	29	116	30.30	0
B. Adults	58	6	20	15	99		
A + B	87	35	49	44	215		
	72 Hour Readings						
A. Children	29	30	29	30	118	38.52	0
B. Adults	52	4	7	34	97		
A + B	81	34	36	64	215		
	96 Hour Readings						
A. Children	30	30	30	30	120	20.59	
B. Adults	49	8	14	23	94		
A + B	79	38	44	53	214		
	Maximum Reaction Areas						
A. Children	30	30	30	30	120	19.09	0
B. Adults	45	33	11	11	100		
A − B	75	63	41	41	220		

* Chi-square = (total A) (total B) 0.004218727 = 116 × 100 × 0.004218727 = 48.13.
N = the number of free cells in the table (one for each quartile) = 4.

varied in limits equal to those observed at this same period for each corresponding quartile of children were also determined, and the results obtained are recorded in the first division of tables 2 and 3 so as to permit a direct comparison of the reactions of persons in each age group to injections of comparable doses of the same test material.

The data for the forty-eight, seventy-two and ninety-six hour periods as well as the readings for the maximum size which the reactions attained [3] were treated in a similar manner, and the averages obtained are given in the remaining sections of tables 2 and 3.

The areas of the Mantoux reactions to old tuberculin at the twenty-four hour reading for the first, or least allergic, quartile (25 per cent)

TABLE 3.—*The Distribution of the Adults, Using the Quartile Range of the Areas of Reaction (Purified Protein Derivative 0.0001 Mg.) for the Children as a Norm and the Significance of the Difference Noted (Chi-Square)*

	Number of Adults with Areas Falling Within the Limits Noted for Each Quartile of Children						
	Quartiles						
	1	2	3	4	Total	Chi-Square N = 4*	Chances per Thousand for the Differences to Arise by Accident (P)
	24 Hour Readings						
A. Children, 8 to 17 years	29	29	29	29	116	111.12	0
B. Adults, 20 to 84 years	96	1	1	2	110		
A + B	125	30	30	31	216		
	48 Hour Readings						
A. Children	29	29	29	29	116	10.92	12
B. Adults	40	28	21	10	99		
A + B	69	57	50	36	215		
	72 Hour Readings						
A. Children	29	30	29	30	118	15.35	2
B. Adults	38	11	36	13	98		
A + B	67	41	65	43	216		
	96 Hour Readings						
A. Children	30	30	30	30	120	4.50	216
B. Adults	35	17	18	25	95		
A + B	65	47	48	55	215		
	Maximum Reaction Areas						
A. Children	30	30	30	30	120	45.00	0
B. Adults	70	12	8	10	100		
A + B	100	42	38	40	220		

* See footnote to table 2.

of the entire group of children ranged from 0.3 to 2.5 sq. cm.[4] Sixty-seven per cent of the adults (67 patients) showed reaction areas that fell within these limits (table 2). This section of the table shows also that the number of adults with areas of reaction to this material which ranged in the limits observed at the first twenty-four hour readings for each of the three remaining quartiles of children amounted to 22, 8 and 3, respectively. Computations based on these observations yield a value of 48.13 for chi-square, which indicates, when N, the number

4. Determined from the individual data and not shown in the tables.

of free cells in the table (one cell for each quartile) equals 4, that no chances exist for the difference in the distribution of different degrees of tuberculin sensitivity observed in the two age groups at the time of the first twenty-four hour reading to be the accidental result of sampling. Similar computations based on the measurements taken at twenty-four hours for the purified protein derivative (table 3) and for each test material at forty-eight and seventy-two hours (tables 2 and 3) as well as the data for the maximum readings [3] also show that the distribution of different degrees of allergy in children differs significantly (chi-square values are below 50 per thousand) from that in adults. The only exception to this general rule was noted in the records made on the reactions to purified protein derivative at the ninety-sixth

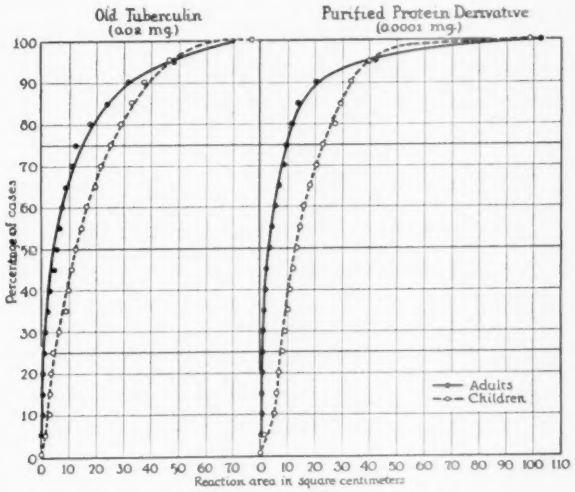

Fig. 2.—Graph showing the maximum areas of the Mantoux reactions.

hour after the tests were made. In this instance there were 216 chances per thousand for the differences to be due to accident, and consequently the difference cannot be interpreted as significant.

In general, however, the conclusion seems justified that the distribution of different degrees of sensitiveness of the skin to tuberculin in children is not identical with that in adults. The difference noted in this respect between the two age groups seems to consist mainly in the occurrence in infected adults of a disproportionally large percentage of patients showing relatively small areas of reaction to tuberculin.

In order to portray the character of the distribution of different degrees of allergy, as expressed in terms of the areas of Mantoux reactions in children and in adults, cumulative frequency curves were constructed from the readings for the two age groups for the maximum size attained by each reaction area (fig. 2). These maximum readings

were selected as indicating the person's true status relative to his degree of sensitiveness to tuberculin, as compared with that of other members of the group. The curves representing this serial arrangement of the data, made in accordance with increasing degrees of allergy, illustrate the difference existing between children and adults relative to the manner in which sensitivity to tuberculin is distributed in each age group. In addition to showing a preponderance of relatively small reactions in adults, the curves also disclose sensitivity to tuberculin to be a highly variable condition fluctuating in area limits the extremes of which are practically equal for all age groups.

CONCLUSIONS

Mantoux tests with old tuberculin and purified protein derivative in doses of unequal potency agree in showing: (*a*) that as a rule children are more sensitive to tuberculoprotein than adults and (*b*) that this difference between the two age groups is due to the occurrence among adults of a disproportionately large percentage of patients with relatively small areas of reaction to tuberculin.

The suggestion is offered that the difference in allergy noted between the two age groups is the product of a general tendency for sensitiveness to tuberculin to diminish slowly as the postinfection time elapses.

The sensitiveness to tuberculoprotein induced in the tissues by tuberculous infection is an extremely variable and moderately unstable immunologic change.

DISTURBANCE OF GASTRO-INTESTINAL INNERVATION IN POLIOMYELITIS

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CLEVELAND

Typhoid fever may sometimes cause paralysis of the muscles of the thigh, probably as a result of the spread of the typhoid toxins from the intestine along the sympathetic to the somatic nerves.[1] Natural protection is such that only patients who are extremely ill with the disease have muscular weakness, an extraordinary fact when one considers the amount of toxic material contained in the intestines of these patients. Since toxins from colon bacilli are considered to be much less potent for the human being than are those from Bacillus typhosus, one does not expect that the toxins from the colon bacilli will spread along the afferent or efferent sympathetic fibers and cause local paralysis by involvement of the somatic nerves. The validity of this assumption was proved by the fact that the injection of enteric toxins into the subserosa or into the lumen of the small intestine of Macacus rhesus monkeys did not cause paresis or paralysis. (Each experiment was performed on two animals.)

Since I believe that in the Macacus rhesus monkey the disease is produced only when the virus factor is combined with the toxic factors that are present as the result of intestinal stasis, i. e., enteric toxins,[2] I thought it logical to ascertain whether the combination of toxin and virus could be prevented. It occurred to me that alcohol might be used to neutralize the virus factor, since the intracerebral injection into monkeys of a combination of 70 per cent alcohol and virus, although it resulted in almost immediate alcoholic paresis and blindness, did not cause poliomyelitis in two animals; the same animals did not possess immunity, since they contracted the disease after subsequent intracerebral injections of poliomyelitis virus. The obvious place to stop the spread of the virus from the cord to the gastro-intestinal tract is somewhere between the cord and the intestine. One method of arresting the spread would be to inject 70 per cent alcohol into the mesenteric nerves in the hope that it would neutralize the virus. Clearcut results

From the department of Pediatrics, Western Reserve University, and the Division of Contagious Diseases, City Hospital.

1. Toomey, John A.: Reflex Changes in Typhoid Fever, Am. J. Dis. Child. **48**:1296 (Dec.) 1934.

2. Toomey, John A.: Intranasal or Gastro-Intestinal Portal of Entry in Poliomyelitis, Science **82**:200, 1935.

could not be expected from this procedure, since it might give rise to apparent paradoxes for the following reasons: (1) The alcohol might be locally absorbed long before all the virus could be destroyed, and (2) the injection of 70 per cent alcohol into the mesenteric nerves might cause a paralysis of intestinal movement with a resulting absorption of the products of intestinal stasis, which was the factor that in previous experiments accelerated the production of the disease.[3] Thus, although the occurrence of poliomyelitis might not be prevented, the incubation period might be prolonged. As a preliminary experiment, I found that blocking the superior and inferior mesenteric nerves with an injection of 70 per cent alcohol did not per se cause a paralytic disturbance of the lower extremities of three monkeys. When the alcohol was injected between the mesenteric folds, the nerves almost immediately stood out like grayish-white fibrous ramifications, which could easily be traced to the intestinal wall.

The next experiments were planned with a view of introducing the virus intracerebrally and of injecting a small amount of 70 per cent alcohol into the superior and inferior mesenteric nerves at the same time or a few days later, when, theoretically, the virus should have reached the lower cord.

Two Macacus rhesus monkeys were given injections intracerebrally of 2 cc. of 5 per cent suspension of poliomyelitis virus; within forty-eight hours 3 cc. of 70 per cent alcohol was injected between the mesenteric folds along the ramifications of the superior mesenteric nerve on both sides of the mesentery, and 2 cc. along the branches of the inferior mesenteric nerve at the base of the large colon. Two monkeys were used as controls. The two animals which had received injections of alcohol became ill on the eighth and ninth day, respectively, and died on the twenty-second and the twenty-fourth day following the injections; the two controls, on the other hand, showed furring on the fourth and the fifth day, respectively, were definitely paralyzed on the seventh day and died on the tenth and the eleventh day, respectively. Although no definite conclusions could be drawn from these experiments, the animals did react in the direction that was theoretically held possible.

The experiment was repeated, but the virus was introduced by way of the gastro-intestinal tract. The same amount of alcohol was injected in the manner described previously, and 50 cc. of a 5 per cent suspension of poliomyelitis virus in saline solution was introduced subserosally into the first set of two animals.

Set 1.—Monkey A, protected by alcohol, was active until the eleventh day after the protection, when tremor and paresis of the left foot developed. It suddenly died from pneumonia on the twelfth day, before paralysis set in.

Monkey B, unprotected by alcohol and kept in the cage with monkey A, was inactive; furring and weakness of the left leg and right foot developed twenty-four hours after the injection. Complete quadriparesis occurred on the third day, and the animal died of the disease on the eleventh day.

3. Toomey, John A.: Accelerated Production of Poliomyelitis, Proc. Soc. Exper. Biol. & Med. **31**:1015, 1934.

SET 2.—Monkey C was protected with alcohol and then was given an injection subserosally of a 10 per cent suspension made up of 20 cc. of poliomyelitis virus combined with 20 cc. of saline solution. Although the animal had some paresis of the right foot on the fifth day, it was active until the twenty-third day, when quadriparesis developed; quadriplegia occurred on the twenty-fourth day and death on the twenty-seventh day.

Monkey D, unprotected, was given an injection subserosally of a 10 per cent suspension made up of 20 cc. of poliomyelitis virus and 20 cc. of saline solution. It was inactive; furring occurred within the first twenty-four hours after the injection, paresis of the legs developed on the second day and quadriplegia on the fifth day, and death occurred on the nineteenth day.

Five other animals and an equal number of controls were similarly treated, and although all ten animals contracted poliomyelitis, there seemed to be a slight delay in the production of the disease in those that had been given injections of alcohol, in spite of the fact that they had had complete anesthesia for over thirty minutes, had been subjected to an abdominal operation and had been given injections into the mesenteric nerves. It was obvious that the surgical procedure itself did not accelerate the production of the disease when the operation was performed at the same time or within a few days after the intracerebral injection of the virus.

What would be the effect, however, if monkeys were operated on and given injections into the mesenteric nerves some time before the virus was injected intracerebrally? If the monkeys were prepared this way, would they not gradually become saturated with the enteric toxins? Were this so, would not the virus of poliomyelitis, if it were injected intracerebrally later, be activated and its effect accelerated?

At intervals, each of four animals, weighing on an average 4½ pounds (2 Kg.), was operated on through the abdominal wall, and 5 cc. of 70 per cent alcohol was injected along the branches of the superior and inferior mesenteric nerves on both sides of the mesentery; then the abdomen was closed. Simultaneously, on the thirteenth, fourteenth, fifteenth and eighteenth postoperative day, respectively, the animals and the two controls were given injections intracerebrally of 1.5 cc. of a 10 per cent suspension of poliomyelitis virus. In all the animals that were operated on hemiparesis was noted on the side opposite that of the intracerebral injection within twenty-four hours. In the two controls there was no furring until the fifth day, and paralysis was not observed before the sixth day.

Since no observations were made on the blood serum or stools of these animals, the experiments were repeated. Five animals were bled and the agglutinin titer of the blood serum against enteric organisms was found to be between 1:160 and 1:320. (The animals selected for this experiment were healthy. They had not had diarrhea recently and were not grossly infested with worms, nor were worm eggs found in the specimens of stools. I mention this fact since monkeys with massive infestations invariably have enteritis.) The stools, from which emulsions were made, were prepared in the same concentrations and amounts as have been

previously described [4] and were injected into five guinea-pigs (weight, 250 Gm. each). Only local induration resulted.

Three of these monkeys were operated on, and alcohol was injected into the mesenteric nerves in the manner described in the foregoing paragraphs. Thirteen days later the stools were tested again. There was no change in the toxicity of the stools of the two controls, but emulsions made from the stools of the three animals that were operated on produced cystic lesions in the abdominal walls of guinea-pigs and caused their death within from twenty-four to thirty-six hours after the injection. The agglutinin titer of the blood serum of the control monkeys against the enteric organisms remained the same, but that of the animals that were operated on showed a decided drop, the new titer ranging from 1:40 to 1:60. On the fourteenth day, after 70 per cent alcohol had been

Protocol *

	Group of Monkeys Given Mesenteric Injections			Control Group	
Date	444 (3,237 Gm.)	445 (2,692 Gm.)	446 (2,670 Gm.)	453 (2,078 Gm.)	454 (2,308 Gm.)
4/24/35	Right hemiparesis; sick; furred	Weak right arm and right foot; furred	Right arm weak; sick; furred	Active; furred	Active; little furred
4/25/35	Tremor; paralysis of right side; very sick	Right side almost completely paralyzed	Inactive; wobbly; right hemiparesis	Active	Active
4/26/35	Very sick; same	Very sick; same	Same and paresis of left foot	Active	Active
4/27/35	Quadriplegia	Quadriplegia	Paresis of both legs and right arm; very ill	Active	Active
4/28/35	Quadriplegia	Quadriplegia	Quadriplegia	Active	Active
4/29/35	Died	Quadriplegia	Quadriplegia	Tremor; left foot weak	Tremor; active
4/30/35	.....	Died	Died	Both lower extremities paralyzed	Paresis of lower extremities
5/ 1/35	.....	.....	.....	Quadriplegia; eating well	Lower extremities paralyzed; paresis of upper extremities
5/ 2/35	.....	.....	.....	Quadriplegia; eating well	Quadriplegia; eating well

* On April 10, 1935, monkeys 444, 445 and 446 were operated on and were given injections of 5 cc. of 70 per cent alcohol about the superior and inferior mesenteric ramifications. Monkeys 453 and 454 were used as controls. On April 23, 1935, all five monkeys were given intracerebral injections on the left side of 2 cc. of a 2 per cent virus suspension. On May 7, 1935, monkeys 453 and 454 were killed.

injected into the mesenteric nerves, all five animals were given injections intracerebrally of 2 cc. of a 2 per cent virus mixture. The effect was the same as that described for the preceding group. The details of this experiment are contained in the protocol.

The same result followed the subsequent intracerebral injection of virus into seven other animals prepared in the same manner. In additions, and this confirms previous experiments,[4] every specimen of stool that was obtained during the prostration stage of the disease from control animals or from those that had been given injections of alcohol

4. Toomey, John A.: Demonstration of a Toxic Factor in the Stools and Urines of Poliomyelitis Patients, J. Prev. Med. **6**:379, 1932.

was toxic to guinea-pigs. Likewise, as has been shown,[5] every specimen of blood serum withdrawn three days after the prostration stage of experimental poliomyelitis showed almost complete absence of agglutinins for enteric organisms.

COMMENT

The dose (2 cc.) was not a factor in producing the hemiparesis in the monkeys, since a sufficient number of them had been given intracerebral injections in these and in other experiments to demonstrate the fact that the massive dose accelerated only slightly, if at all, the production of the disease, and then only when planned injections were made directly into the motor area. Even in this experiment the effect was not permanent. The usual incubation period of from six to ten days elapsed before paralysis developed, whether the dose was 0.2 cc. of a 1 per cent virus suspension or 2 cc. of a 10 per cent virus suspension, and there was always a free interval between the injection and the development of paralysis. In the experiments described, however, there was an immediate hemiparesis in the animals in which the motility of the gastro-intestinal tract was disturbed. Previously, it was shown that the intracerebral injection of a suspension consisting of the toxic filtrates of enteric organisms combined with the virus of poliomyelitis caused an immediate heterolateral paresis or paralysis.[3] Likewise, it has been shown that when the filtrate of enteric toxins and the bacteria themselves were injected into baby Macacus rhesus monkeys, they became saturated with these products, so that when the virus was introduced later the production of the disease was accelerated.[6] One might conjecture that the animals that were prepared, as described, by the injection of alcohol between the mesenteric folds had paralysis of the intestine and as a result actually became saturated with the toxic products of the enteric organisms and other poisons from the intestines; therefore, when subsequent intracerebral injections of virus were made, I merely duplicated, in another way, the experiment referred to previously.[3]

CONCLUSIONS

Hemiparesis did not occur in animals that had alcohol injected into their mesenteric nerves a few days before or after the intracerebral injection of the virus. In fact, although the monkeys on whom operation had been performed contracted the disease, it developed a little

5. Toomey, John A.: Changes in Titers of Agglutinins for Enteric Organisms in the Blood Serum in Poliomyelitis, J. Infect. Dis. **54**:74, 1934.

6. Toomey, John A.: Effect of Poliomyelitis Virus in Baby Monkeys Previously Given Paratyphoid Colon Filtrate and Vaccine, Proc. Soc. Exper. Biol. & Med. **32**:869, 1935.

later in them than in the controls, which had neither been operated on nor given injections.

In animals that were prepared by an injection of alcohol into the mesenteric nerves some time previous to a subsequent intracerebral injection of virus hemiparesis developed after the latter event, as it did in those animals that had been given intracerebral injections of doses of the combined paratyphoid-colon bacillus filtrate (enteric toxin) and virus.[3]

EXTENT AND NATURE OF THE DECLINE OF TUBERCULOUS INFECTION IN CHILDREN

AN ANALYSIS OF DATA CONCERNING 4,982 CHILDREN TESTED WITH OLD TUBERCULIN DURING THE YEARS FROM 1926 TO 1934 INCLUSIVE

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ROCHESTER, N. Y.

Workers interested in tuberculous infection in children are aware that its incidence, measured either by clinical signs or by the presence of a positive reaction to tuberculin, has been decreasing. It has been my impression that this decline has been felt in Rochester and that the severity of the infection itself has been decreasing. This analysis was undertaken to determine the annual incidence of tuberculous infection here and the annual percentage of children with positive reactions to tuberculin who show clinical or roentgenologic evidence of the disease. Any change may in a manner determine whether the virulence of the organism has altered.

GENERAL CONSIDERATIONS

Since 1926, when the Strong Memorial Hospital and the Rochester Municipal Hospital first admitted patients, a tuberculin test of all children admitted to the pediatric division has been a routine. The children referred to in this study are from this group. In determining the annual distribution of patients, the hospital records allot each patient to the year in which he was discharged. This is the method used in this report. In case of subsequent admission in later years, the patient is not included again. The exception to this is the child who on first admission had a negative reaction and on a subsequent admission had a positive reaction. Such a child is allotted to the year in which he first manifested a positive reaction.

The ages of the children studied range from birth through the fourteenth year. There were 4,982 children. Of this number, 480, or 9.6 per cent, had tuberculous infection. Of those who had tuberculous infection, 40, or 8.3 per cent, died of tuberculosis. This is not a mortality rate for two reasons: The final outcome of the condition in all positive reactors is not known. The patients who died came to the hospital with meningitis or with miliary tuberculosis, and the figures

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represent really the rate of deaths from tuberculosis in that part of the community served by the two hospitals. There were 16 children in addition among the group having positive reactions to old tuberculin who died of nontuberculous diseases.

The children with tuberculous infection were native born almost without exception. It may be helpful in comparing this with similar studies to note that 19.7 per cent of the patients were of Italian parentage, 5.8 per cent were from Jewish families and 3.5 per cent were Negroes.

TYPE AND TECHNIC OF THE TUBERCULIN TESTS

The routine procedure in testing was the Mantoux method. One-tenth cubic centimeter of a 1:1,000 dilution of old tuberculin with physiologic solution of sodium chloride was injected intracutaneously into the forearm. A positive reaction was indicated by an area of redness and induration approximately 1 cm. in diameter. Although the area tested was examined at the end of twenty-four hours, forty-eight hours and five days, only those patients were included in the group having positive reactions whose reactions indicated sensitivity to tuberculin at the forty-eight hour reading. Nearly all the reactions that were positive were so on all three readings. Those who were shown to be sensitive to tuberculin at the end of twenty-four hours only were not included unless when retested with stronger dilutions they were shown to have positive reactions after the forty-eight hour interval. There were no patients whose reaction was negative on the first two readings and positive on the fifth day.

The Mantoux test was used consistently, except that in 1926 some of the children were tested by the Pirquet scratch method and that 2 children with tuberculous meningitis were given no test.

All tuberculous children tested had positive reactions with the exception of 5 with tuberculous meningitis. Two of these were given a 1:1,000 dilution of old tuberculin, 1 was given a 1:10,000 dilution, 1 was given a 1:1,000 dilution three days before death and 1 was given a 1:1,000 dilution four days before death. Had these children been tested before they were moribund or with a stronger concentration of old tuberculin (an unnecessary procedure from a diagnostic point of view), they undoubtedly would have given a positive response. This conclusion seems justified by the work of Happ and Casparis [1] and Hart [2] in a larger series of cases of tuberculous meningitis. For this reason and for the sake of brevity all the tuberculous children are referred to as having positive reactions to old tuberculin.

SCOPE OF SURVEY

This report is divided into six parts: (1) analysis of the relationship of all children tested to those having a positive reaction to tuberculin; (2) analysis of the data concerning the group of children with positive

1. Happ, W. M., and Casparis, H. R.: The Value of the Intracutaneous Test in Extensive Tuberculosis, Am. J. Dis. Child. **23**:527-530 (June) 1922.

2. Hart, P. D'Arcy: Value of Tuberculin Test in Man, with Special Reference to the Intra-Cutaneous Test, Medical Research Council, Special Report Series, no. 164, London, His Majesty's Stationery Office, 1932, p. 51.

reactions, without regard to the year in which the reaction appeared; (3) review of literature showing a decrease in tuberculous infections in other cities and in rural districts; (4) analysis of the data concerning the group with positive reactions to tuberculin in this survey arranged annually and in three year periods; (5) annual analysis of the data concerning the group having roentgenologic evidence of tuberculosis and concerning those having clinical signs of tuberculosis, and (6) analysis of the relationship of these data to the existence of reported clinical tuberculosis occurring in the children of the community and in adults in the community and to deaths from tuberculosis in the community.

TABLE 1.—*Analysis of Number and Percentage of All Children Tested with Old Tuberculin, Showing Age Incidence*

Age	Total Tested		Children Having Positive Reactions to Old Tuberculin			Children Having Positive Reactions to Tuberculin with Clinical or Roentgenologic Evidence of Tuberculosis			Group That Died of Tuberculosis		
	Number	Percentage	Number	Percentage		Number	Percentage		Number	Percentage	
1	928	18.6	15	1.6		9	60		6	40.0	
1 to 2	571	11.4	9	1.6		5	55.5		5	55.5	
2 to 3	430	8.7	29	6.9	4.4	15	51.8	52	6	20.0	23.1
3 to 4	368	7.4	34	9.2		15	44.1		5	14.7	
4 to 5	345	6.9	28	8.1		16	57.3		5	17.8	
5 to 6	310	6.2	31	10.0		17	54.9		5	16.1	
6 to 7	330	6.7	31	9.4		15	48.4		2	6.4	
7 to 8	273	5.5	37	13.6		16	43.3		1	2.7	
8 to 9	270	5.4	43	16.0		15	34.9		1	2.3	
9 to 10	249	5.0	45	18.1		21	46.8		0	0	
10 to 11	245	4.9	36	14.7	15.6	12	33.3	41.2	0	0	3.6
11 to 12	199	4.0	36	18.1		17	47.2		1	2.8	
12 to 13	186	3.7	33	17.7		14	42.4		1	3.0	
13 to 14	150	3.0	42	28.0		10	23.9		0	0	
14 to 15	128	2.6	31	24.0		13	41.9		2	6.4	
Totals and gen. avers.	4,982		480	9.6		210	43.6		40	8.3	

ANALYSIS OF THE RELATIONSHIP OF ALL CHILDREN TESTED TO THOSE HAVING A POSITIVE REACTION TO TUBERCULIN

Age.—Table 1 shows that the majority of the children tested were quite young. The largest number were under 1 year, and with advancing age the total number tested gradually decreased, the fewest being in the fourteenth year.

On the other hand, the majority of the positive reactors were in the older age group. Positive reactions occurred only in 1.6 per cent of the total number of children tested in their first year. The number gradually increased until in the fourteenth and fifteenth years the percentage of children with positive reactions to old tuberculin was 28 and 24, respectively, of the total number of children tested. The general average incidence was 9.5 per cent. This tendency for the evidence of

infection to increase with advancing age has been noted by all observers. The percentage of positive reactors, however, was lower in this series than in groups surveyed in other urban areas.

Comparative Surveys in Other Cities

Author	Place	Year	Per-centage	Year	Per-centage	Average Incidence, Percentage
Dickey and Seitz[3]	San Francisco	First	5.6	Fourteenth	46.6	23.5
Smith[4]	New York	First	5.2	Twelfth	43.4	16.8
Drolet[5]	New York	First	4.4	Fourteenth	42.1	14.0
Johnston and Chadwich[6]	Detroit	First	1.7	Fourteenth	16.7	14.3
Webb[7]	Chicago	First	3.5	Fourteenth	30.5	14.5
Beaven	Rochester	First	1.6	Fourteenth	24.2	9.5

Comparative Surveys in Rural Areas.—A detailed comparison of age groups in Rochester with those in rural areas is difficult, since surveys in rural areas have included only school children. However, if the children of school age in this study are subdivided, as in table 1, a comparison can be made, as follows:

Author	Place	Age	Average Incidence, Percentage
Slater and Jordan [8]	Rural Minnesota	School children	13.3
Korns [9]	Cattaragus County, N. Y.	School children	10.2
Beaven	Rochester, N. Y.	5 to 14 years	15.6

The increase of the evidence of tuberculous infection with advancing age shown in this report is analogous to the findings of other workers. The general incidence of positive reactions to old tuberculin is somewhat lower than those reported in larger cities and higher than those reported in the rural districts.

Relationship of Age to Clinical or Roentgenologic Evidence of Tuberculosis.—Table 1 shows that in this series of cases a positive

3. Dickey, L. B., and Seitz, R. R.: The Incidence of Tuberculous Infection in 3,500 Children as Based on the Intracutaneous Tuberculin Tests, Am. Rev. Tuberc. **23**:13-22 (Jan.) 1931.

4. Smith, C. H.: Tuberculin Skin Reactions, Am. J. Dis. Child. **38**:1137-1154 (Dec.) 1929.

5. Drolet, C. J.: Childhood Tuberculous Infection in New York, Am. Rev. Tuberc. **30**:1-32, 1934.

6. Johnston, J. A., and Chadwick, H. D.: A Study of Childhood Tuberculosis in Detroit, Am. Rev. Tuberc. **28**:244-250 (Aug.) 1933.

7. Webb, C. H.: Skin Reactions and Tuberculous Disease in Children, Am. Rev. Tuberc. **26**:583-585 (Nov.) 1932.

8. Slater, S. S., and Jordan, K. A.: Comparative Study of the Pirquet and Mantoux Tests in School Children, Am. Rev. Tuberc. **25**:218-223 (Feb.) 1932.

9. Korns, J. H.: Tuberculous Infection Among School Children in a Rural Area in New York State, Am. Rev. Tuberc. **24**:532-536 (Nov.) 1931.

reaction to tuberculin in a child 5 years of age or under in 52 per cent of cases carries with it the implication that such a child possesses clinical or roentgenologic evidence of tuberculosis. In children from 6 to 14 years of age the incidence is 41.2 per cent. At all ages in childhood 43.5 per cent of the children with a positive reaction will show clinical or roentgenologic evidence of the disease. Table 1 also shows the ages at which most children die of tuberculosis. The percentage of deaths among the children infected was 23.1 per cent at the age of 5 years and under and only 3.6 per cent between the ages of 6 and 14 years. This is comparable with the observations of Rich and McCordock [10] and Wallgren.[11]

TABLE 2.—*Sex of All Children Tested with Old Tuberculin*

Age	Whole Group Tested				Group with Positive Reactions to Old Tuberculin				Children Dying of Tuberculosis			
	Boys		Girls		Boys		Girls		Boys		Girls	
	Number	Percentage	Number	Percentage	Number	Percentage	Number	Percentage	Number	Percentage	Number	Percentage
1 to 4 inclusive	1,431	54.2	1,211	45.8	63	55.4	52	44.6	15	55.5	12	44.5
5 to 9 inclusive	711	49.6	721	50.4	86	45.6	101	54.6	4	44.4	5	55.6
10 to 14 inclusive	467	51.4	441	48.6	93	52.2	85	47.8	3	75.0	1	25.0
Totals and general averages	2,609	52.3	2,373	47.7	242	50.3	238	49.7	22	55.0	18	45.0

Sex.—It is a curious but universally noted fact that in any children's ward boys are more numerous than girls. It was so in this study. In the group having positive reactions to old tuberculin this is slightly apparent, though the difference is negligible (table 2). An even distribution between the sexes of positive reactions was observed by Drolet [5] and by Myers and Harrington.[12]

Although this is a very small series, the number of boys dying was greater than the number of girls. In Drolet's analysis of 143 deaths from tuberculosis in white children, he observed that 62 per cent occurred in boys. This is of significance, since Zachs [13] has pointed out that in the next age period, adolescence, the higher mortality is found in girls. In summary, although tuberculous infection is about equally distributed between boys and girls, in early childhood the boy is more likely to die.

10. Rich, A. R., and McCordock, H. A.: Pathogenesis of Tuberculous Meningitis, Bull. Johns Hopkins Hosp. **52**:5-30, 1932.

11. Wallgren, A.: Some Aspects of Tuberculous Meningitis and the Possibility of Its Prevention, J. Pediat. **5**:291-298 (Sept.) 1934.

12. Myers, J. A., and Harrington, F. E.: The Effect of the Initial Tuberculous Infection on Subsequent Lesions, J. A. M. A. **103**:1530-1536 (Nov. 17) 1934.

13. Zachs, D.: What We Have Learned in Massachusetts from the Ten Year Program, New England J. Med. **205**:525-531 (Sept. 10) 1931.

ANALYSIS OF THE DATA CONCERNING THE GROUP OF CHILDREN WITH POSITIVE REACTIONS, WITHOUT REGARD TO THE YEAR IN WHICH EACH INSTANCE APPEARED

Nutrition.—Children in the wards were not weighed and measured as a routine to determine the nutrition. A statement was made, however, as to whether a patient was well nourished, fairly well nourished or poorly nourished. Table 3 shows that the children with tuberculous infection were in general well nourished. This observation was also made by Barnard, Amberson and Loew [14] in a report from New York. If one classifies the children having positive reactions according to their degree of evident infection, one notes these differences:

Eighty per cent of the children with no clinical or roentgenologic evidence of tuberculosis were well nourished (271 cases). Seventy-six

TABLE 3.—*Analysis of Nutrition of Children Having Positive Reactions to Old Tuberculin*

	All Children with Positive Reactions		Positive Reactions to Old Tuberculin but no Clinical or Roentgenologic Evidence of Tuberculosis		Positive Reactions to Old Tuberculin with Clinical or Roentgenologic Evidence of Tuberculosis		Tuberculous Meningitis and Miliary Tuberculosis	
	Number	Percentage	Number	Percentage	Number	Percentage	Number	Percentage
Well nourished.....	375	78.2	218	80.8	161	76.6	27	67.5
Fairly well nourished..	16	3.3	7	2.6	9	4.3	2	5.0
Poorly nourished.....	89	18.5	45	16.6	40	19.1	11	27.5
Total.....	480		270		210		40	

per cent of the children with clinical or roentgenologic evidence of tuberculosis were well nourished (210 cases).

Nutrition was affected, though not to a great extent, by tuberculous infection.

Exposure.—Table 4 shows that approximately 25 per cent of the group having positive reactions to old tuberculin were known to have been exposed to tuberculosis. Other workers have reported higher and lower incidences. For example, Barnard and his co-workers [14] noted an incidence of known exposure of only 9 per cent in a group of 184 adolescents known to have tuberculosis. On the other hand, Martin,[15] in Oakland, Calif., reported known contacts in 67 per cent of 60 young children known to have tuberculosis. The table shows that there is a direct relationship between "known exposure" and the development of roentgenologic signs or other symptoms of tuberculosis. In 270 children

14. Barnard, W.; Amberson, J. B., Jr., and Loew, M. F.: Tuberculosis in Adolescents, Am. Rev. Tuberc. **23**:593-641 (May) 1931.

15. Martin, A.: Tuberculous Pulmonary Infiltration in Childhood, Am. J. Dis. Child. **44**:754-769 (Oct.) 1932.

having positive reactions to old tuberculin, with no clinical or roentgenologic evidence of tuberculosis, the incidence of known exposure was 13.8 per cent. In 210 tuberculous children with clinical or roentgenologic signs, the incidence of known exposure was 38.2 per cent. Of those examined in this survey, a child with known exposure was three times as likely to acquire clinical or roentgenologic evidence of the disease as a child with no known exposure.

With exceptions, no known exposure means casual exposure, and known exposure means intimate contact with some tuberculous person. Interpreted in this way, the fact is brought out that, in general, the more continuous the exposure to tuberculosis, the more likely is clinical or roentgenologic evidence of the disease to develop. If this is true, any annual variation in the number of exposed children would probably

TABLE 4.—*Analysis of Tuberculous Children with Known Exposure and No Known Exposure*

Years	Total Tuberculous Children				Tuberculous Children with no Clinical or Roentgenologic Evidence				Tuberculous Children with Clinical or Roentgenologic Evidence			
	No Known Exposure		Known Exposure		No Known Exposure		Known Exposure		No Known Exposure		Known Exposure	
	Number	Percentage	Number	Percentage	Number	Percentage	Number	Percentage	Number	Percentage	Number	Percentage
1926, 1927, 1928	158	81.8	35	18.2	108	91.6	10	8.4	50	66.6	25	33.4
1929, 1930, 1931	132	71.3	53	28.7	79	81.5	18	18.5	53	60.2	35	39.8
1932, 1933, 1934	73	71.5	29	28.5	46	83.6	9	16.4	27	57.4	20	42.6
1926 to 1934	363	75.6	117	24.4	233	86.2	37	13.8	130	61.8	80	38.2

result in a similar annual variation in the number of children showing either roentgenologic evidence or clinical symptoms of tuberculosis.

In order to determine whether such a variation in the children known to have been exposed existed, in table 4 is given a similar analysis in three year periods for the total nine years. Thus in 1926, 1927 and 1928, 33.4 per cent of 75 children with positive reactions to old tuberculin and with clinical or roentgenologic evidence of tuberculosis were known to have been exposed. In 1929, 1930 and 1931, 39.8 per cent of 88 children were known to have been exposed. In 1932, 1933 and 1934, 42.6 per cent of 47 children were known to have been exposed.

There was a slight increase over the nine years in the incidence of known exposure of children who had clinical or roentgenologic signs of tuberculosis. This factor may be accounted for by better history taking. It is possible, however, that it is related to the fact, brought out later in this paper, that there is a slight increase in the number of tuberculous children who show clinical or roentgenologic symptoms of infection when the data were analyzed annually over the nine year period.

In summary, the more continuous or intimate the exposure, the more likely is the child to show clinical or roentgenologic signs of tuberculosis. It is also true that during the years of this study the incidence of known exposure in the children who have clinical or roentgenologic evidence of tuberculosis has remained fairly constant. The small variation which existed was a slight increase, which may be related to a similar increase in the number of children showing clinical or roentgenologic evidence of tuberculosis when the data were analyzed annually during the period of this study.

REVIEW OF THE LITERATURE, SHOWING DECLINE IN TUBERCULOUS INFECTION IN OTHER CITIES

Table 5 shows that Myers and Harrington [12] in 1934 called attention to the fact that the annual incidence of positive reactions to tuberculin in Minneapolis children had undergone a marked decline. They published the annual percentages of children reacting positively from 1922 to 1933. Their report in part is shown in the table. With the exception of this survey to determine the declining spread of tuberculous infection elsewhere, it is necessary to combine observations made in one year or set of years with similar observations made in later years, in some instances by the same author and in others by different authors.

Table 5 gives an instance in Trondhjem. In 1914 Arnfinsen [16] found that 38 per cent of 6,978 school children had a positive Pirquet reaction; fifteen years later Ustvedt [17] found in a similar group of 4,719 school children that 23.5 per cent had positive reactions. This is a decrease of over 38 per cent.

A second example is in Framingham, Mass. Chadwick and Zachs [18] reported that in the tuberculosis survey of 1917 in that town, 33.3 per cent of 460 young children reacted positively to the Pirquet test. Nine years later they tested 520 older children, who because of their age would be expected to have a higher incidence of tuberculous infection. They found that less than 25 per cent of 520 children gave positive reactions. The decrease was 25.5 per cent.

In 1921 Myers and Harrington [12] reported a 41.6 per cent incidence in the first 1,000 children examined at the University of Minnesota, the Pirquet test being used. The average incidence for children in this clinic in 1933 was 23.6 per cent, a decrease of 43 per cent.

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16. Arnfinsen, A.: Cutireactions (von Pirquet Tests) Among the School Children of Trondhjem, Norsk mag. f. lægevidensk. **80**:508-531, 1919.

17. Ustvedt, H. J.: Dwindling Number of Pirquet Reactions in School Children, Tidsskr. f. d. norske lægefor., Nov. 1, 1930, p. 1187; abstr., Brit. M. J. **2**:1056 (Dec. 20) 1930.

18. Chadwick, H. D., and Zachs, D.: The Incidence of Tuberculous Infection in School Children, New England J. Med. **200**:332-337 (Feb. 14) 1929.

TABLE 5.—*Analysis of Decrease of Incidence of Positive Reactions to Old Tuberculin in Children of Other Cities*

	First Tests							Second Tests							
	Year	Locality	Author	Age Group Tested	Number Children	Type Test	Percentage of Positive Reactions	Year	Locality	Author	Age Group Tested	Number Children	Type Test	Percentage of Positive Reactions	Percentage Decrease
1	1914	Trondhjem, Norway	Arnfinsen [16]	School children	6,978	Pirquet	38	1929; interval 15 yrs.	Trondhjem, Norway	Ustvedt [17]	School children	4,719	Pirquet	23.5	38.2
2	1917	Framingham, Mass.	Chadwick and Zachs [18]	Age 4 to 7	460	Pirquet	33.3	1926; interval 9 yrs.	Framingham, Mass.	Chadwick and Zachs [18]	Age 10 to 14	520	Pirquet	24.8	25.5
3	1921	Minneapolis	Myers and Harrington [12]	School children	1,000	Pirquet	41.6	1933; interval 12 yrs.	Minneapolis	Myers and Harrington [12]	School children	Annual admission at University Hospital	Mantoux	23.6	43
4	1921 to 1928	New York	Smith [4]	65 per cent under 5 yrs. age 1 to 14	7,668	Mantoux	16.8	1930 to 1932; mean interval 7 yrs.	New York	Drolet [5]	23 per cent 5 yrs. and under; age 1 to 14	8,085	Mantoux	14.0	10.7
5	1923	Minneapolis	Stewart [19]	1 to 19	Annual admission at Lymanhurst	Mantoux	30	1933; interval 10 yrs.	Minneapolis	Stewart [19]	1 to 19	1,091	Mantoux	13	57
6	1925 to 1928	San Francisco	Dickey [3]	Evenly distributed 1 to 14	3,500	Mantoux	23.5	1929; mean interval 3 yrs.	Detroit	Johnston and Chadwick [6]	Evenly distributed; 1 to 14	2,467	Mantoux	14.3	39.0
								1930 and 1931; mean interval 5 yrs.	Chicago	Webb [7]	Evenly distributed; 1 to 14	1,000	Mantoux	14.5	38.0
7	1926 to 1928	Rochester, N. Y.	Beaven	1 to 14; average age 5.3 yrs.	1,783	Mantoux	14.8	1932 to 1934; mean interval 7 yrs.	Rochester, N. Y.	Beaven	1 to 14; average age 4.8 yrs.	2,798	Mantoux	5.6	62.1

Smith [4] analyzed the incidence of positive reaction to old tuberculin in 7,668 children attending the Bellevue Hospital from 1921 to 1928. The great majority of his patients were young, 65 per cent being under 5 years of age. He found that 16.8 per cent gave positive reactions. The 1930, 1931 and 1932 admissions to the Bellevue Hospital, the New York Nursery and Child's Hospital and St. Luke's Hospital, and seven clinics for well babies were reviewed by Drolet.[5] He found that 10.7 per cent of the children of his group had positive reactions, although older than those in Smith's, as only 23 per cent were under 5 years of age. The decrease was 10.7 per cent.

Stewart [19] stated that in 1933 the percentage of positive reactors in 1,091 children at the Lymanhurst School for Tuberculous Children in Minneapolis was 13. Ten years previously the annual percentage was 30, the decrease being 57 per cent.

Dickey and Seitz [3] performed a Mantoux test on 3,500 children in San Francisco during the years from 1925 to 1928. The ages were evenly distributed in the first 14 years of life; 23.5 per cent had positive reactions. In 1929 Johnston and Chadwick [6] studied 2,467 children in Detroit with the same age distribution. The percentage of positive reactions was 14.3. In 1931 Webb [7] reported tuberculin tests on 1,000 children of the same age group in Chicago. He reported that 14.5 per cent gave positive reactions. The decrease shown in these later observations as compared with the San Francisco survey was 39 per cent in Detroit, and 38 per cent in Chicago. The excellent report by Hetherington and his co-workers [20] in 1929, giving an analysis of children with positive reactions to tuberculin in Philadelphia, is omitted because of the high percentage of Negroes among the children. In all the reports given in table 5, the percentage of Negroes is low.

If the data for the first three years of our study are grouped, and also those for the last three years, it is seen that there was a decrease in the incidence of positive reactions in Rochester in the last seven years of 62.1 per cent.

ANALYSIS OF THE DATA CONCERNING THE CHILDREN IN THE GROUP WITH POSITIVE REACTIONS TO TUBERCULIN ARRANGED ANNUALLY AND IN THREE YEAR PERIODS

The number of children in this group is given in one year periods and in three year periods in table 6.

19. Stewart, C. A.: Old Tuberculin, Human Tubercle Bacillus Protein and Trichloracetic Acid Precipitate, Am. J. Dis. Child. **49**:625-637 (March) 1935.

20. Hetherington, H. W.; McPhedran, F.; Landis, H. R. M., and Opie, E. L.: A Survey to Determine the Incidence of Tuberculosis Infection in School Children, Am. Rev. Tuberc. **20**:421-510 (Oct.) 1929.

TABLE 6.—*Distribution of All Children Tested and of Those Having Positive Reactions to Old Tuberculin*

	Total Number of Children Tested	Total Number of Children with Positive Reactions to Old Tuberculin
One Year Periods		
1926	226	51
1927	468	81
1928	507	61
1929	510	74
1930	724	60
1931	745	51
1932	593	40
1933	583	41
1934	626	21
Three Year Periods		
1926, 1927, 1928	1,201	193
1929, 1930, 1931	1,979	185
1932, 1933, 1934	1,802	102

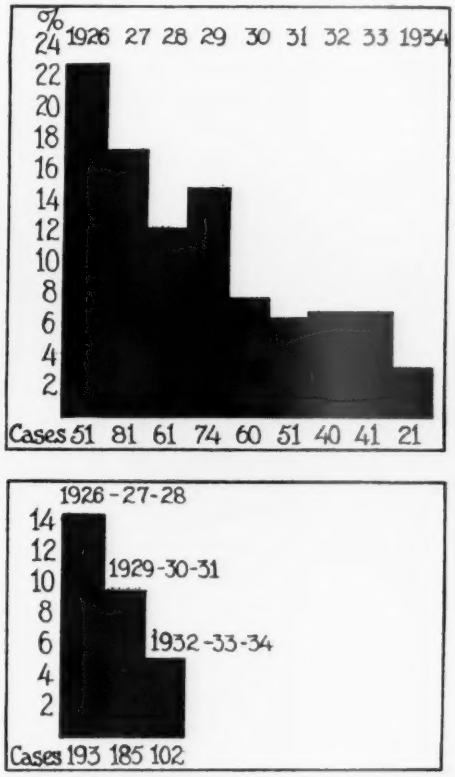

Chart 1.—Percentage of positive reactions to tuberculin in all children tested, arranged by one year periods (upper chart) and by three year periods (lower chart).

Percentage of Children with Positive Reactions in One Year and Three Year Periods.—Chart 1 gives the annual decrease in the incidence of positive reactions to old tuberculin children. In 1926 it was 22.6 per cent; in 1934, 3.5 per cent. When arranged in three year periods in order to include a larger number of children in the tuberculous group, the data show: In 1926, 1927 and 1928 the percentage was 14.8; in 1929, 1930 and 1931 it was 9.4; in 1932, 1933 and 1934 it was 5.6.

Average Age of Group with Positive Reactions in One Year and in Three Year Periods.—Since age is an important factor in the incidence of tuberculous infection, it is important to know whether the group age of the children tested varied from year to year. Chart 2 shows that

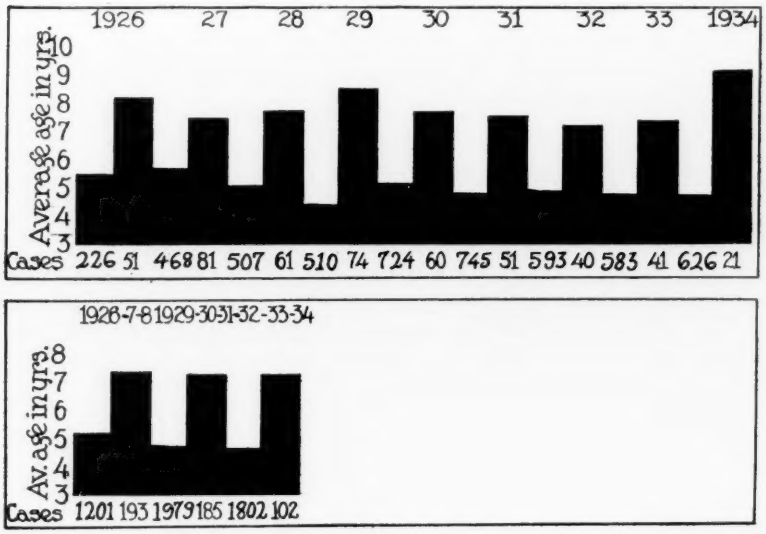

Chart 2.—The average age in years of the whole group of children tested and of the children who reacted positively to tests with old tuberculin. The upper chart shows the annual variation, and the lower chart shows the variation for three year periods. The first column under each period indicates the average age of all children tested, and the second column indicates the average age of all children giving positive reactions to old tuberculin in the same period.

there was no variation of any importance in the group reacting to old tuberculin when the data were arranged annually and none at all when they were arranged in three year periods. For the same reason it is necessary to determine the average age of the whole group tested. The chart shows that there was no variation. In these nine years the average group age of the ward population has remained fairly constant, and the average group age of the children having positive reactions to old tuberculin has remained entirely so, showing that there is no tendency

for tuberculous infection to attack older or younger children, its age incidence remaining the same.

Decline of Incidence of Tuberculosis in Each Age Group in Three Year Periods.—While the average age of the children affected might remain the same, it is still true that there might be a decrease at one age and an increase at another. In order to determine whether this was the case, chart 3 was constructed. An analysis by age was made at the end of each three year period. The percentage decline at each age between the first three years and the last three years is shown to be approximately the same. If ages are computed in groups from 1 to 4 inclusive, 5 to 9 inclusive and 10 to 14 inclusive, they show a decline of 67 per

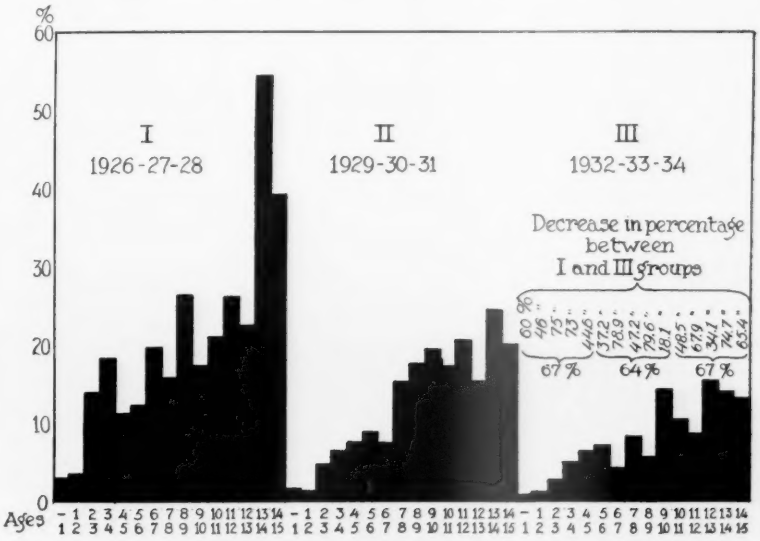

Chart 3.—Incidence of positive reactions to old tuberculin for each year of age arranged in three year periods. The average percentage of positive reactions in the first period was 14.8, in the second period 9.4 and in the third 5.6.

cent, 64 per cent and 67 per cent, respectively, between the first and the last group. It is apparent that the rate of decline in the incidence of tuberculous infection is the same at all ages of childhood.

Annual Percentage of Children Having Clinical or Roentgenologic Evidence of Tuberculosis.—Charts 4 and 5 analyze this relationship for one year and for three year periods. The chart shows that the percentage of children in the group having positive reactions to old tuberculin who show clinical or roentgenologic signs of tuberculosis is rising slightly. It also shows that the number of children who have not had roentgenologic examinations is decreasing year by year. It is possible that this accounts in some measure for the increase, since some of these

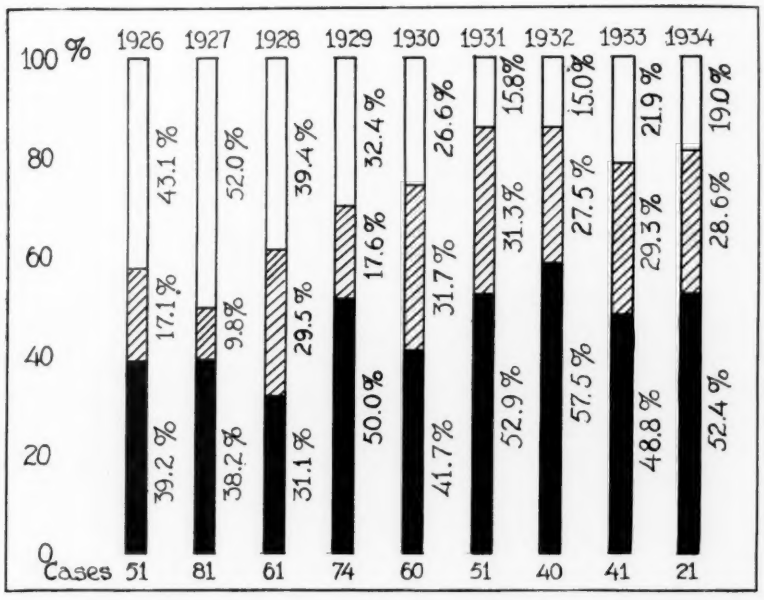

Chart 4.—Analysis of data concerning groups of children with positive reactions to old tuberculin for one year periods, showing the percentage having clinical or roentgenologic evidence of tuberculosis. In this chart and in chart 5 the unshaded portions indicate the percentage of children with no clinical evidence of tuberculosis. Roentgenograms were not made in these cases. The diagonal shading indicates the percentage showing no clinical evidence and having negative roentgenograms. Solid shading indicates the percentage in whom there was either clinical or roentgenologic evidence of infection.

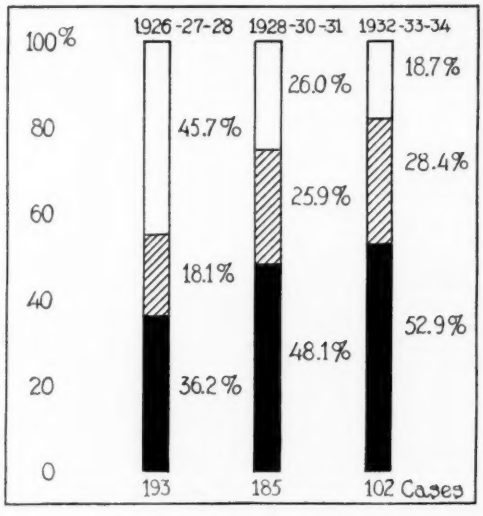

Chart 5.—Analysis of data concerning groups of children with positive reactions to tuberculin for three year periods, showing the percentage having clinical or roentgenologic evidence of tuberculosis.

children might have shown roentgenologic evidence of the disease. However, Myers and Harrington [12] called attention to the fact that the incidence of roentgenologic evidence of pulmonary infection in children with positive reactions to old tuberculin rose in a group which they studied during approximately the years involved in this study. The chart shows that there is no decrease in the number of children showing clinical or roentgenologic evidence of tuberculosis, but indeed a slight increase, once a child has become infected.

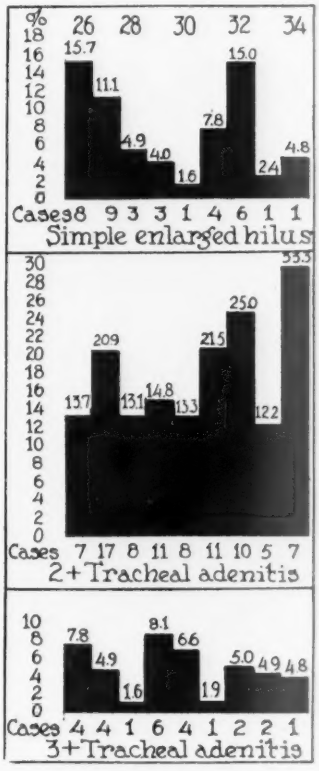

Chart 6.—Annual incidence of different types of tuberculosis in children with positive reactions to old tuberculin. The diagnoses were made from roentgenograms.

ANALYSIS OF THE DATA CONCERNING THE GROUP HAVING ROENTGENOLOGIC EVIDENCE AND CLINICAL SIGNS OF TUBERCULOSIS

Tuberculosis with Positive Roentgenologic Signs.—Dr. J. H. Green, of the department of radiology of the University of Rochester School of Medicine and Dentistry, reviewed all the plates referred to in this report. The incidence of positive signs of tuberculosis annually is given. Individual children might present more than one diagnosis. Tracheal adenitis

was graded 1, 2 or 3 plus; 1 plus was considered questionable, and data for children with this degree of involvement were left out. Chart 6 shows that there is no drop in the incidence of enlarged hili or 2 plus or 3 plus tracheal adenitis. Primary tuberculosis of the lung was definitely greater in incidence in the last five years. The number of children showing the adult type of tuberculosis or the presence of a Ghon tubercle was too small to be of significance in the one year periods.

Tuberculosis with Clinical Signs.—Chart 8 shows that the incidence of tuberculous pleural effusion was slightly higher in the last four years, and this is also true of tuberculous meningitis. The patients with miliary

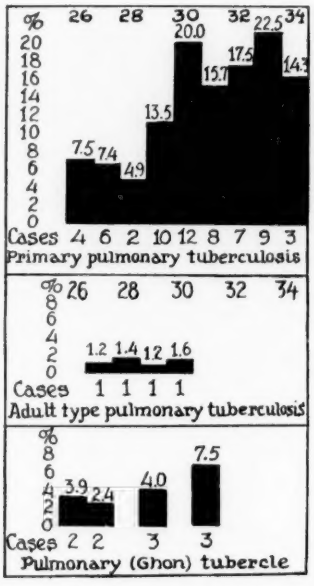

Chart 7.—Annual incidence of different types of tuberculosis in children with positive reactions to old tuberculin. The diagnoses were made from roentgenograms.

tuberculosis were too few to be of significance in the annual distribution. However, attention may well be called to the fact that the children in whom the disease ended fatally all had miliary tuberculosis or tuberculous meningitis. Deaths from these types of the disease were as frequent as ever within the group with positive reactions to old tuberculin. The tubercle bacillus is therefore just as fatal to children as it ever was.

The percentage of cases of cervical adenitis appears to be about the same year after year. Tuberculous peritonitis, arthritis and those diseases which are possibly of tuberculous origin, phlyctenular conjunctivities, erythema nodosum and chronic bronchiectasis, occurred so few times that annual distribution has little meaning (charts 9 and 10).

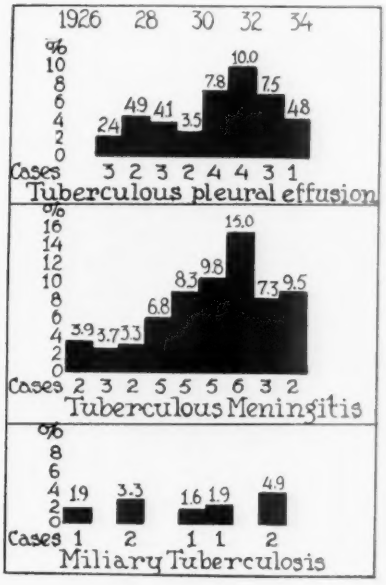

Chart 8.—Annual incidence of different types of tuberculosis in children with positive reactions to old tuberculin. The diagnoses were made from clinical evidence.

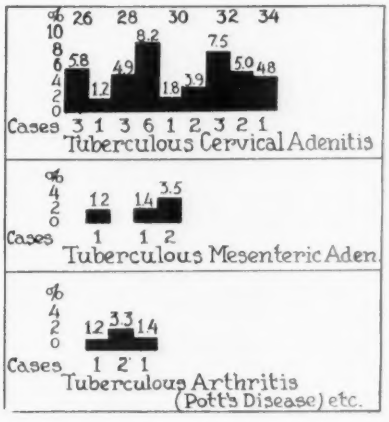

Chart 9.—Annual incidence of different types of tuberculosis in children with positive reactions to old tuberculin. The diagnoses were made from clinical evidence.

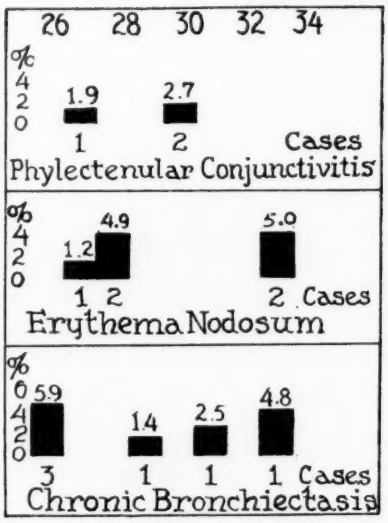

Chart 10.—Annual incidence of different conditions which were possibly tuberculous in children with positive reactions to old tuberculin. The diagnoses were made from clinical evidence.

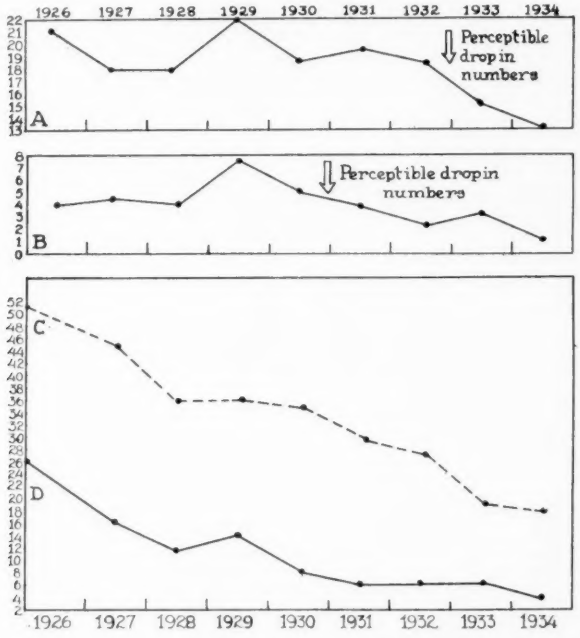

Chart 11.—Relationship of annual incidence of positive reactions to old tuberculin in children in the hospital to the annual mortality from tuberculosis in Rochester, N. Y. The curve at *A* indicates the number of reported cases of tuberculosis in persons over 14 years of age per ten thousand of population. The curve at *B* indicates the number of reported cases of tuberculosis in persons under 14 years of age per ten thousand of population. The curve at *C* indicates the annual number of deaths from tuberculosis of persons of all ages per hundred thousand of population. The curve at *D* indicates the annual incidence of positive reactions to old tuberculin in children in the wards of hospitals per hundred of population.

RELATION OF THE INCIDENCE OF TUBERCULOUS INFECTION TO THE INCIDENCE OF REPORTED CASES OF TUBERCULOSIS IN CHILDREN AND IN ADULTS AND TO DEATHS FROM TUBERCULOSIS IN THE COMMUNITY

In chart 11 the curve representing the deaths from tuberculosis of all types and the curve representing the incidence of tuberculosis of all types in children roughly parallel one another.

The similarity is not as marked in the curves showing the incidence of reported cases of tuberculosis in the child and adult population of Rochester, N. Y. A factor which must be considered is that during the past ten years a great effort has been made to induce physicians to report every case observed. The failure of the curves to come down earlier is probably due to the fact that a greater proportion of cases of tuberculosis have been reported recently. In spite of this, there was a perceptible drop in the number of reported cases of tuberculosis in adults in 1933 and 1934. A similar perceptible decline occurred in the children's group beginning in 1931. During the time covered by this survey there has been a drop in the incidence of tuberculous infection in the hospital wards and a similar drop in the death rate from tuberculosis in the community. There was also a drop, but not as marked, in the number of reported cases of tuberculosis in both children and adults in the community.

COMMENT

In 1935 Boynton [21] made a report of the annual number of deaths from tuberculosis in the state of Minnesota during the years from 1915 to 1932. She pointed out that the number of deaths per hundred thousand of population decreased year by year, showing a 58 per cent total decrease during that period. During the same years in Rochester, N. Y., there has been a total decrease in the number of deaths from tuberculosis of 74 per cent.[22]

The decrease in deaths in Minnesota has been shown by Myers and Harrington [12] to have been attended by a similar decline of the number of positive reactions to tuberculin in a group of children in Minneapolis. This report shows that the decrease in deaths from tuberculosis in Rochester, N. Y., was attended by a similar decrease in two of the hospitals in this city.

Arnfinsen [16] said: "The greater the spread of tuberculous infection (a positive tuberculin reaction) the lower is the mortality from tuber-

21. Boynton, R. L.: The Declining Death Rate from Tuberculosis in Children, J. A. M. A. **104**:1875-1878 (May 25) 1935.

22. Mortality records of the Rochester Health Bureau. These data and those referred to in curves *A*, *B* and *C* in chart 11 are contained in personal communications to the author from Dr. A. M. Johnson, Health Officer of Rochester, N. Y.

culosis." This would follow if the presence of a positive cutaneous reaction indicated immunity. This survey and the work of Boynton and of Myers in Minnesota show that if there is a decline in the rate of tuberculous infection as shown by a positive reaction to tuberculin, there will be a lower rate of mortality from tuberculosis.

In the first paragraph of this paper it was stated that the known decline in the morbidity and mortality from tuberculosis might be due to the attenuation of the organism itself. It is difficult to measure the virulence of the tubercle bacillus by clinical standards, since many factors are involved in any evaluation of this kind. Such factors are: (1) the magnitude and repetition of infection, (2) the age of the infected person, (3) the limitations of diagnosis and (4) the personal equation involved in the reading of roentgen films.

If it can be shown that whatever modifications may result from any of these factors are the same year after year and if a record is made of a rise or fall in the clinical manifestations or roentgenologic evidence of pathologic conditions within the group having tuberculous disease, a fair estimate of the virulence of the organism may be made.

It is well known that if a child is in contact with a person who spreads large numbers of tubercle bacilli he is likely to acquire the infection, even though the contact is short. It is equally well known that continuous contact with a person who spreads even small numbers of bacilli will almost surely result in tuberculosis in a child. In discussing exposure in this group it was shown that such children not only will acquire the infection but are much more likely to have a pathologic condition in the chest which can be revealed by the roentgenogram. This condition was shown to be present constantly throughout the nine years of this survey. It was even slightly more pronounced in the later years of the study. To summarize, the reaction to the tubercle bacillus, as influenced by degree or by repetition of infection, was equally potent or perhaps increasingly potent throughout these observations.

It is also known that the younger the child the more certain he is to show symptoms. This is a universal observation and was true of the children in this study. This was stated in discussing the age of the whole group studied. If there had been a decrease in the whole group age, then symptoms from infection would naturally increase. This, however, was not the case and cannot influence the percentage of children showing symptoms or positive roentgenologic findings.

It is recognized that any division of tuberculous children into those who show symptoms and signs of infection and those who do not show them is in reality an artificial distinction. A patient with a positive cutaneous reaction has tuberculosis and all the prognostic implications that go with such an infection. When roentgen examination gives negative results at a given time, it does not follow that the patient

always has been or will be normal. It does not even follow that the pulmonary fields are then normal. It simply means no pathologic change was noted by the reviewer. What is true of roentgenologic diagnosis is equally true of clinical symptoms. When examined, the child may have had symptoms previously or may acquire them later. These observations, however, are equally true for every year included in this report and modify the results equally. If during the course of this study the tuberculous children had shown fewer symptoms and a decrease in the number of positive roentgen signs, it could be assumed that the organism was not as virulent, provided the other factors referred to did not modify these observations. What actually occurred was, as the charts indicate, that there was a slight annual increase in the percentage of tuberculous children showing signs and symptoms of this infection.

The final factor which must always be taken into consideration is the personal equation involved in reading the roentgen films. In order to eliminate this as much as possible, the interpretation of the films appearing on the charts was not used, as these had been made by different physicians. The interpretations of the films which appear in this paper were made by one physician, at the same time, and his opinion only was used in making a statement of diagnosis.

It is clear that all these factors indicate that the tubercle bacillus during the course of this survey has lost none of its virulence. It is the same organism, attacking the same age group, acting in the same way when amount and repetition of infection are factors, creating the same pathologic condition and producing a similar mortality.

SUMMARY

Tuberculin tests on 4,982 children admitted to the Children's Division of the Strong Memorial Hospital and the Rochester Municipal Hospital during the years from 1926 to 1934 (inclusive) are analyzed. Four hundred and eighty of these children, or 9.6 per cent, had positive reactions.

The ages of the children studied were from 1 to 14 years (inclusive). The larger number were in the earlier age group.

The number of children having a positive reaction to old tuberculin increases as age advances.

The significance of a positive reaction is greater in the younger child. Fifty-two per cent of all children from 1 to 5 years (inclusive) having a positive reaction to old tuberculin had clinical or roentgenologic evidence of tuberculosis. In children from 6 to 14 years (inclusive) such evidence was present in 41.2 per cent of cases.

Death from tuberculosis occurs much more frequently in the age group from 1 to 5 years inclusive.

A positive reaction to old tuberculin in a child has approximately an equal occurrence in the two sexes, but boys are more likely to die.

In children tuberculosis affects the nutrition but slightly.

Known exposure in a child is in general synonymous with continued exposure and is directly related to the seriousness of the disease. In the series studied tuberculous children with no signs or symptoms of the disease showed an incidence of 13.8 per cent of known exposure while those with clinical or roentgenologic evidence of the disease had an incidence of known exposure of 38 per cent. In the latter children the percentage increased slightly during the years included in this study.

The decline in the proportion of children with positive reactions to old tuberculin during the course of this survey was 62 per cent. Other communities show a somewhat similar decline.

This decline in the incidence of tuberculous infection in children has not been attended by any change in the age incidence of the disease during these nine years.

The rate of decline in the number of tuberculous children has been equal at all ages in childhood.

During the period studied, once a child had a positive reaction to tuberculin, there was no tendency for the disease to be less severe. On the contrary, in the last three or four years infection with the tubercle bacillus has been more likely to result in positive clinical signs or in positive roentgenologic evidence than earlier in this survey.

The mortality rate among infected children has changed little.

Many factors are involved in an attempt to estimate the present virulence of the tubercle bacillus. However, when they are taken into consideration, it seems clear that the evidence points at this time to the conclusion that the virulence of the bacillus has not declined during the period covered by this report.

The decrease in the number of children with positive reactions to tuberculin has been attended by a similar decrease in the number of deaths from tuberculosis in Rochester, N. Y. It has also been attended by a decline in the number of reported cases of clinical tuberculosis, both in children and in adults, in this community.

CONCLUSION

Tuberculosis among children is decreasing rapidly. If the rate of decline continues, it will soon be a rare disease. This is apparently happening not because of any attenuation in the virulence of the organism causing tuberculosis but because fewer persons are infected with this organism.

STUDIES IN WHOOPING COUGH

DIAGNOSIS AND IMMUNIZATION

LEILA DAUGHTRY-DENMARK, M.D.
ATLANTA, GA.

Three hundred thousand [1] is a conservative estimate of the annual number of cases of whooping cough in this country, and the disease is responsible for 15 per cent of the deaths among infants whom it attacks. The great need for a method of early diagnosis, for effective quarantine and for preventive measures for those who have been exposed has been stressed.[2]

The problem that presents itself may therefore be summarized as follows:

1. What aid in diagnosis may be expected from hematologic studies? Can a typical blood picture be produced with pertussis vaccine?

2. Will agglutination tests assist in early diagnosis?

3. Does the blood of patients with whooping cough show complement fixation with Bacillus pertussis as the antigen?

4. If complement fixation is present with whooping cough, is it possible to produce it artificially?

5. If complement fixation can be produced artificially, does it confer immunity against whooping cough?

6. Is it possible to improve the present pertussis vaccine?

OBSERVATIONS

Hematologic Studies.—In 56 cases of whooping cough a white blood cell count and a differential count were made each week for six weeks. The results are shown in chart 1. The leukocyte counts ranged from 7,000 to 80,000. The 80,000 count occurred an hour before death. Excluding this unusually high figure, the

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Read before the Fulton County Medical Society, Feb. 20, 1936.

The clinic was conducted at the Central Presbyterian Clinic for Children.

Eli Lilly & Co. furnished the vaccine and suspension and also the cultures of the living organisms for use in all my experimental work.

The laboratory work was done in Dr. Roy R. Kracke's laboratory at Emory University. Dr. T. F. Sellers and the staff of the Georgia State Public Health Laboratory also collaborated.

1. Annual Epidemiological Report of the Health Section of the League of Nations, Geneva, International Labour Office, 1935.

2. Toomey, J. A.: A Statistical Analysis of Whooping Cough Cases, J. Pediat. **5**:322 (Sept.) 1934.

average count was 17,800. The percentage of lymphocytes ranged from 31 to 90, averaging 72. It will be seen that the increase in leukocytes was due essentially to an increase in lymphocytes.

In chart 2 a comparative study of the blood pictures of 340 patients receiving vaccine and of 56 patients with whooping cough is presented. It will be noted that the average white cell count was 11,000 with 60 per cent lymphocytes in 240 cases after the use of Sauer's vaccine; 14,800 with 71 per cent lymphocytes in 100 cases after the use of double strength pertussis vaccine, and 17,800 with 72 per cent lymphocytes in 56 cases of whooping cough. No difference in results was noted after vaccination whether the vaccine was less than one week or more than four months old.

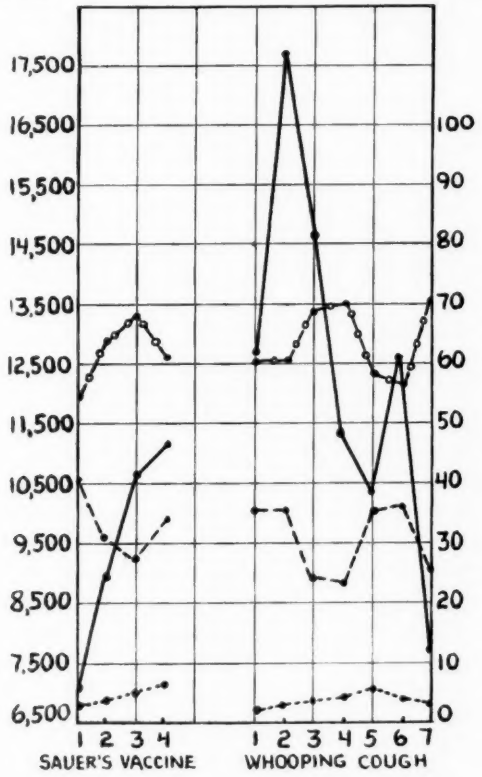

Chart 1.—Comparative study of the blood pictures of 240 patients with conditions other than whooping cough who received vaccine (at left) and of 56 patients with whooping cough from the catarrhal stage through seven weeks (at right). The curves at the left show the white blood cell counts and differential counts (*1*) before vaccination, (*2*) one week after the administration of 2 cc. of vaccine, (*3*) one week after the administration of 3 cc. of vaccine and (*4*) one week after the administration of a second 3 cc. of vaccine. The curves at the right show the white blood cell counts and differential counts (*1*) one week before whoop developed, (*2*) after the first week of whoop and (*3* to *7*) through the seventh week. The numbers at the left represent leukocytes; those at the right, differential percentages. The solid line represents leukocytes; the dash line, polymorphonuclears; the circle and dash line, lymphocytes, and the dotted line, eosinophils.

In chart 3 the blood counts are presented according to age groups. It will be noted that the relatively high percentage of lymphocytes in infants was increased by the vaccine.

Agglutination Tests.—Ten children with whooping cough and 50 children who had not had whooping cough were selected for agglutination tests. There was often spontaneous microscopic agglutination without serum. After the addition of serum, there was microscopic agglutination in 75 per cent of all cases. Macroscopically there was incomplete agglutination in all cases. This study was continued for one month after the 50 children had received pertussis vaccine.

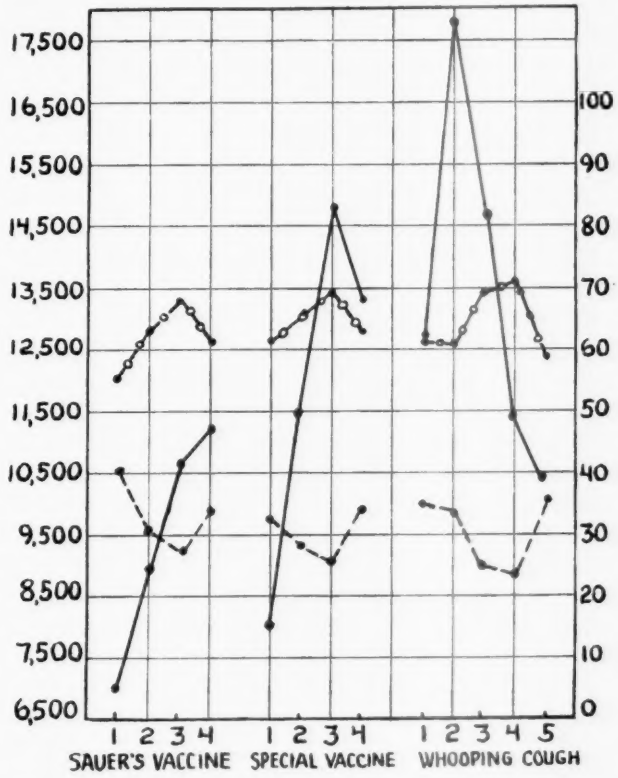

Chart 2.—Comparative study of the blood pictures of 240 patients who were given Sauer's vaccine, 100 who were given the special vaccine and 56 with whooping cough. The first and second groups of curves show the white blood cell counts and differential counts (*1*) before vaccination, (*2*) one week after the administration of 2 cc. of vaccine, (*3*) one week after the administration of 3 cc. of vaccine and (*4*) one week after the administration of a second 3 cc. of vaccine. The third group of curves shows the white blood cell counts and differential counts (*1*) one week before whoop developed, (*2*) after the first week of whoop and (*3* to *5*) through the fifth week. The numbers at the left represent leukocytes; those at the right, differential percentages. The solid line represents leukocytes; the dash line, polymorphonuclears, and the circle and dash line, lymphocytes.

There was no evidence of a specific agglutinin in any case. The Georgia State Public Health Laboratory later conducted agglutination tests for me in another series of 50 cases, and the results were equally inconclusive.

Complement Fixation Tests in the Diagnosis of Whooping Cough.—The clinic for diagnosis and treatment admitted 76 patients, 56 of whom had whooping cough. When the diagnosis was made, the children were segregated. Blood counts and complement fixation tests were made at each weekly visit. The technic used for the complement fixation test was the same as that employed for the Wassermann test; B. pertussis, 10 billion organisms per cubic centimeter, was used as the antigen.

As shown in chart 4, one week before the whoop developed there was positive fixation in 94.1 per cent of the cases and complete fixation in 11.7 per cent. In the first week of whooping there was positive fixation in 100 per cent and complete fixation in 79.1 per cent. In the fourth week there was positive fixation in 100 per cent and complete fixation in 98.9 per cent.

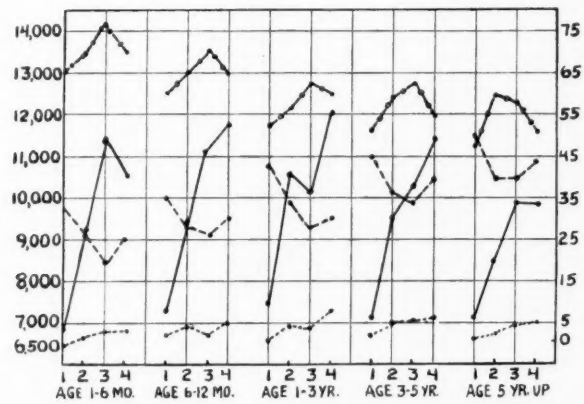

Chart 3.—Comparative study of the blood pictures of patients of different ages who were given Sauer's vaccine. The curves, arranged according to age groups, show the white blood cell counts and the differential counts (*1*) before vaccination, (*2*) one week after the administration of 2 cc. of vaccine, (*3*) one week after the administration of 3 cc. of vaccine and (*4*) one week after the administration of a second 3 cc. of vaccine. The numbers at the left represent leukocytes; those at the right, differential percentages. The solid line represents leukocytes; the dash line, polymorphonuclears; the circle and dash line, lymphocytes, and the dotted line, eosinophils.

At the tenth week I was successful in securing complement fixation tests on the blood of only 11 children. At that time complete fixation was present in only 1 case, and in 2 cases there was no fixation.

Of 50 sophomore college students who had had whooping cough in childhood, there was positive fixation in 4 (8 per cent) and complete fixation in only 1 (2 per cent).

Soon after the clinic was started, a patient was admitted who had been sent home a week before from a day nursery on account of a severe cold and a cough. He had been whooping for two days when he was admitted to the clinic. He had 1 plus complement fixation, but the blood count was not typical. The white

cells numbered 11,750, and the differential count was as follows: polymorphonuclears, 45 per cent; lymphocytes, 50 per cent, and eosinophils, 5 per cent. One week later the complement fixation was 2 plus; the white cells numbered 12,200, and the differential count was as follows: polymorphonuclears, 38 per cent, and lymphocytes, 62 per cent. The patient was whooping and vomiting. It was learned that in the nursery there were 21 children with a cough; several of these had vomited but none had whooped. Blood counts and complement fixation tests were done on all these children, and they were dismissed from the nursery.

In 15 of the cases complement fixation was not obtained and the cough cleared up immediately after treatment. After the second negative test, the 15 children were readmitted to the nursery. However, white cell and differential counts and complement fixation tests were done on all of them, and careful histories were taken as to coughing and vomiting each week for a month.

The other 6 of the 21 patients with severe cough had positive complement fixation, but leukocytosis with an increase in the number of lymphocytes was present in only 2. These children were not readmitted to the nursery for six weeks. In all there developed typical whooping cough. It is difficult to state

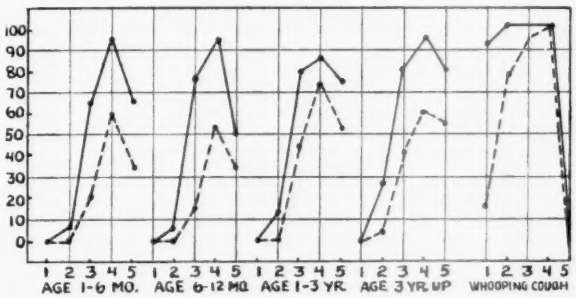

Chart 4.—Comparative study of the complement fixation reactions of patients receiving vaccine and of those with whooping cough. The solid line represents complement fixation, and the broken line, complete complement fixation. The first four groups of curves show complement fixation (*1*) before vaccination, (*2*) one week after the administration of 2 cc. of vaccine, (*3*) one week after the administration of 3 cc. of vaccine, (*4*) one week after the administration of the second 3 cc. of vaccine and (*5*) five months after vaccination. The fifth group of curves shows complement fixation (*1*) during the first week of cough before whoop developed, (*2*) after the first week of whoop, (*3*) after the second week of whoop, (*4*) after the third week of whoop and (*5*) fifteen years after whooping cough.

just how long the 6 children had been coughing because of pertussis, as it was only fourteen days from the time the first child was dismissed from the nursery, and he did not whoop until one week later. None of the children whooped until from four to six days after the first positive test.

Here is another illustrative case:

C. W. J., aged 40, had had a severe cough for three weeks. He had vomited after coughing and had had laryngeal spasms. He was put to bed. After roentgen examination a diagnosis of severe acute bronchitis was made. When he came to my office, the white blood cells numbered 12,000, with a differential count as follows: polymorphonuclears, 36 per cent; lymphocytes, 60 per cent, and eosino-

phils, 4 per cent. The complement fixation reaction was 4 plus. The man had never had whooping cough. One week later his 3 children began to whoop and to vomit after meals.

Complement Fixation Tests After Vaccination.—One hundred and fifty patients, ranging in age from 2 weeks to 7 years, were selected for complement fixation tests after vaccination. Blood was obtained for the complement fixation test and for leukocyte and differential counts; then 2 cc. of vaccine was given. One week later complement fixation tests and blood counts were again made, but this time 3 cc. of vaccine was given. One week later this procedure was repeated. At the fourth week no vaccine was given, but blood was obtained for complement fixation tests and blood counts.

All blood was obtained from the second finger by puncture with a no. 11 Bard-Parker knife; it was easy to obtain from 1.5 to 2 cc. in a small test tube. After centrifugation in the original test tube, the serum was always clear and showed no hemolysis.

The children were seen in the morning. In the afternoon of the same day, a clinic was held for patients with whooping cough. The vaccinated patients were used as controls in a comparative study of the complement fixation test.

The results of the complement fixation test were determined for different age groups to see if there was any difference in the antibody response in persons of different ages. The results are shown in chart 4. It will be seen that the children under 6 months of age showed as marked a response as the older children. A comparison was also made of the antibody response of 25 patients who at the beginning of this study received vaccine that was four months old and of 25 patients who received vaccine not more than three days old. There was no difference in the antibody response in the two groups.

With 8 cc. of vaccine prepared and given according to Sauer's [3] recommendation, complement fixation was obtained in 91.3 per cent of the cases; this was complete in 63.5 per cent. To 11 of the patients whose blood did not give a positive reaction, 3 cc. of vaccine was given two weeks later, and of this number 1 still had a negative reaction, and 1 had a 2 plus, another a 3 plus and 8 a 4 plus reaction. After an additional 3 cc. of vaccine was given, the patient with a negative reaction had a 3 plus reaction. That is, when an extra 3 cc. of vaccine was given a 4 plus complement fixation reaction was obtained in 97.6 per cent of the cases, and after a second additional 3 cc. (a total of 14 cc.) a 4 plus reaction was obtained in 99.2 per cent.

J. B., aged 4 years, and R. B., aged 2 years, brothers, received the same amount of vaccine at the same time—a total of 8 cc. over a period of three weeks. J. B. had a 4 plus fixation after the second injection, and the reaction remained 4 plus after the fourth week. The blood of R. B. did not show complement fixation until the fourth week, at which time the reaction was 1 plus. Three months later they moved into an apartment where they were in contact with a child who had severe whooping cough of two weeks' duration. Three weeks later R. B. (with 1 plus fixation) had typical whooping cough. J. B. (with 4 plus fixation) did not have a cough of any kind.

Using the same type of vaccine and the same type of antigen, the Georgia State Public Health Laboratory performed complement fixation tests for 50 patients from whom I had obtained blood. They found the same percentage of 4 plus

3. Sauer, Lewis: Whooping Cough: A Study in Immunization, J. A. M. A. **100**:239 (Jan. 28) 1933.

reactions as I did, but their percentage of lesser reactions was somewhat higher. This difference could be due to a variation in reading a reaction indicating less than complete complement fixation.

In no case in the whole series was even incomplete complement fixation secured in the absence of whooping cough or of vaccination.

Complement Fixation Tests with Special Vaccine.—Since my work proves that in some cases 11 or even 14 cc. of Sauer's vaccine is required to secure complete complement fixation, at least this much should be administered. To give an adequate amount would require eight or more injections, which would be a considerable burden on the child as well as on the parent. I therefore asked Eli Lilly & Co. to prepare a vaccine with a count of 20 billion. They sent enough vaccine for 100 patients. The first week 1 cc. was injected into each arm, one week later 1.5 cc. into each arm and the third week 1 cc. into each arm. Complement fixation tests were made at weekly intervals until one week after the last injection.

Chart 5 shows a comparative study of the complement fixation reactions of patients given Sauer's vaccine, of those given the special vaccine and of those

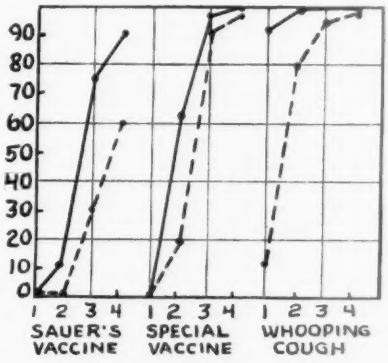

Chart 5.—Comparative study of the complement fixation reactions of patients given Sauer's vaccine, of those given the special vaccine and of those with whooping cough. The solid line represents complement fixation, and the broken line, complete complement fixation. The first and second groups of curves show complement fixation before vaccination, (*2*) one week after the administration of 2 cc. of vaccine, (*3*) one week after the administration of 3 cc. of vaccine and (*4*) one week after the administration of a second 3 cc. of Sauer's vaccine and 2 cc. of special vaccine. The third group of curves shows complement fixation (*1* to *4*) from the first through the fourth week of whooping cough.

with whooping cough. The results for the patients given the special vaccine and those for the patients with whooping cough were the same at the fourth week. With 5 cc. of the special vaccine 93.3 per cent of the children had plus fixation, and with 7 cc., 100 per cent. The systemic and local reactions were approximately the same as those obtained with Sauer's vaccine.

The complement fixation tests in this series were done in the Georgia State Public Health Laboratory.

Follow-Up Studies.—The study of whooping cough which I conducted over a period of about three years included observation of 240 clinic patients who

received Sauer's vaccine. Complement fixation tests were not done in the first 2 groups of patients vaccinated, totaling 109 children. During the past two weeks (Jan. 15, 1936) I have personally seen each of the patients and obtained an accurate history as to exposure subsequent to vaccination and as to the number of patients who had contracted whooping cough.

In the first group, 56 patients vaccinated in May 1933, 37 had direct exposure (direct exposure means that the child was in the home of a patient with whooping cough or played with a child with whooping cough for the duration of the contagious period). Seven patients, ranging in age from 8 months to 7 years, contracted whooping cough. Each patient was seen as soon as the cough developed and was followed closely. Blood counts were made and careful histories were taken to insure correct diagnosis. None had whooping cough in less than three months after vaccination. This would indicate immunity in 81.1 per cent of the cases in which there was direct exposure to whooping cough.

Of the second group, 53 patients vaccinated in September 1934, 7 had direct exposure. In no case did whooping cough develop. In this group, not included in the 7 who had undergone exposure, there were 2 patients who received 2 cc. of vaccine and did not return for the other 2 inoculations. In these 2 whooping cough developed five months later.

Of the third group, 47 patients vaccinated in October 1934, 9 had direct exposure. Eight of the children, who showed complete complement fixation, remained well. The ninth child who had been exposed showed 1 plus fixation and had severe whooping cough.

Of the fourth group, 29 patients vaccinated in January 1935, 9 had direct exposure. In no case did whooping cough develop.

Of the fifth group, 55 patients vaccinated in May 1935, 11 had direct exposure. In no case did whooping cough develop.

No child who received the double strength vaccine was exposed to whooping cough.

COMMENT

1. From hematologic studies it is apparent that in a patient with a severe cough a marked increase in the number of leukocytes with more than 60 per cent lymphocytes indicates whooping cough. However, the absence of such a blood picture by no means excludes the disease; for, although it is not a well known fact, normal leukocyte and differential counts do not disprove the presence of whooping cough.

Sauer reported a marked increase in leukocytes with a relative increase in lymphocytes as a result of vaccination. In my series of 240 patients who received Sauer's vaccine, 4 blood counts being made in each case, there was also an increase in lymphocytes, but it was much less marked. When I used the double strength vaccine, the blood counts of a series of 100 patients were even more typical of whooping cough than those reported by Sauer. This reaction occurred irrespective of the age of the patient; that is, the normally high number of lymphocytes in the infant was increased by the vaccine proportionately as much as was the smaller number of lymphocytes in the older child.

However, the leukocyte and differential counts are not a clear and accurate index to the response of the body to the vaccine, because the counts are so easily influenced by other infections the child may have while taking the vaccine.

2. I have found, and the Georgia State Public Health Laboratory corroborated my experience, that B. pertussis has agglutinated spontaneously both with normal serum and with the serum of patients with whooping cough; and since, moreover, agglutination has never been complete, the test is worthless in the diagnosis of whooping cough.

3. In spite of a great deal of work that has been done in an effort to determine the etiology of whooping cough since Bordet and Gengou described their organism in 1900, the pertussis bacillus has not been universally accepted as the etiologic agent. Rich,[4] for example, stated that the "lesion may be the effect of an invisible virus rather than of secondary bacterial invasion," since the interstitial reaction in the lungs resembles that in measles and in influenza.

Bordet and Gengou in 1906 clearly differentiated the pertussis bacillus from the influenza bacillus and demonstrated in the serum of their patients a positive complement fixation reaction for the pertussis bacillus.

Madsen[5] stated: "Another reason why it is permissible to consider the Bordet bacillus as the cause of whooping cough is the regularity with which the complement fixation appears positive in patients with whooping cough." He found after the first week that the complement fixation reaction gradually increased until from the fifth to the seventh week, after which it decreased slowly.

In 1914 Friedlander and Wagner[6] used a test for determining the complement fixation which enabled them to make the diagnosis of pertussis in all stages. The same year Hess[7] had equal success with a small series of cases.

Olmstead and Povilzky[8] were able to differentiate between the typical or atypical Bordet-Gengou bacillus and the influenza bacillus by complement fixation tests.

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4. Rich, A. R.: On the Etiology and Pathogenesis of Whooping Cough, Bull. Johns Hopkins Hosp. **51**:346 (Dec.) 1932.

5. Madsen, Thorvald: Whooping Cough: Its Bacteriology, Diagnosis, Prevention and Treatment, Boston M. & S. J. **192**:50 (Jan. 8) 1925.

6. Friedlander, Alfred, and Wagner, E. A.: Diagnosis of Whooping Cough by the Complement Deviation Test, Am. J. Dis. Child. **8**:134 (Aug.) 1914.

7. Hess, A. F.: The Use of a Series of Vaccines in the Prophylaxis and Treatment of an Epidemic of Pertussis, J. A. M. A. **63**:1007 (Sept. 19) 1914.

8. Olmstead, A. M., and Povilzky, O. R.: The Complement Fixation Reaction of the Bordet-Gengou Bacillus, J. M. Research **33**:379 (Jan.) 1916.

It is probable that complement fixation as a diagnostic test was used less extensively than it might have been on account of the difficulty of repeated venipunctures on small children. The difficulty was overcome by making a stab wound of the finger.

The present investigation has shown that, although hematologic studies are of value only when the results are positive and that agglutination tests are without value, the complement fixation test may be relied on for the early diagnosis of whooping cough, that is, before the whoop develops. Of 15 children who had been exposed to whooping cough, and who were in the catarrhal stage, with only a mild cough, the complement fixation test was positive for 94 per cent. Of the same group of children, one week later, although the whoop had not yet developed, 100 per cent had positive complement fixation. By the beginning of the third week, at the time the whoop had appeared, 96 per cent of the group had complete fixation. After the eighth week, however, there was a decline in the percentage with complete complement fixation.

Since it is hard to keep the small child coming to the clinic, I have not yet been able to make complement fixation tests after vaccination long enough or in enough cases to give significant figures about the reversal of fixation, but the studies that I have been able to make indicate a trend toward reversal. This trend is also evident in the group of 50 college students who had had whooping cough in childhood. Only 1 of these had 4 plus fixation, and 46 had a negative reaction.

4. Huenekens [9] stated: "Our observation in seventeen cases would theoretically justify the prophylactic vaccination against pertussis. In none of these cases treated with small doses could any antibodies be demonstrated, whereas large doses, such as recommended by the New York City Health Department, showed antibodies in 44 per cent of the cases. The freshly prepared vaccines were apparently more effective than the stock vaccines, as 60 per cent of the patients treated gave positive fixation reaction." He also stated the belief that it is possible to immunize against whooping cough if sufficiently large doses of freshly prepared vaccine are used. Huenekens [10] emphasized again in 1918, the importance of using large doses of fresh vaccine if immunization is to be effected. He stated that the vaccine should not be over a week old. Madsen [11] and Sauer [3] also advocated the use of large doses of fresh vaccine given before exposure.

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9. Huenekens, E. J.: The Prophylactic Use of Pertussis Vaccine Controlled by the Complement Fixation Test, Am. J. Dis. Child. **14**:283 (Oct.) 1917.

10. Huenekens, E. J.: Further Reports on the Use of Pertussis Controlled by the Complement Fixation Test, Am. J. Dis. Child. **16**:30 (July) 1918.

11. Madsen, Thorvald: Vaccination Against Whooping Cough, J. A. M. A. **101**:187 (July 15) 1933.

Sauer's vaccine was administered to 150 children. Complement fixation was secured one week later in 92 per cent and was complete in 61 per cent. All of those who received as much as 14 cc. of vaccine had complete complement fixation. This proves that Sauer's vaccine is effective in producing complete fixation. It may be remarked again that there was no difference in my results whether the vaccine was less than a week old or more than four months old.

5. Thirty-seven children who received Sauer's vaccine in May 1933 were exposed to whooping cough. Seven of these contracted the disease, but in each case it was mild. Seven children who were vaccinated in September 1934 and were exposed to whooping cough remained well.

There have been 9 exposures in the third group, vaccinated in October 1934. The single child who had incomplete complement fixation contracted whooping cough. After this experience each child was given enough vaccine to secure complete complement fixation. Nine children vaccinated in January 1935 and 11 vaccinated in May 1935 have been directly exposed to whooping cough, but in none has the disease developed.

It must be emphasized that 28 children in whose blood complete fixation was secured by the use of Sauer's vaccine were directly exposed to whooping cough and did not contract the disease. In several cases the exposure was immediate. This indicates that the vaccine becomes effective as soon as complement fixation is secured, instead of three months after administration, as has been suggested.

Sauer has expressed the opinion that his vaccine will confer lasting immunity. It is too early to confirm this. My studies have demonstrated that children who have whooping cough have complete complement fixation during the disease but may have no fixation a few months later. The same condition is true of vaccine. If one may reason by analogy, the immunity conferred by vaccination may last as long as that conferred by the disease.

SUMMARY

A normal blood picture does not disprove the presence of whooping cough. Double strength vaccine produces a leukocytosis with an increase in the percentage of lymphocytes that approaches the increase observed in typical whooping cough.

Agglutination tests are without value in the diagnosis of whooping cough.

Complement fixation tests, B. pertussis being used as the antigen, are positive in more than 90 per cent of cases of whooping cough even before the severe cough develops.

It is possible to secure complete complement fixation by the use of Sauer's pertussis vaccine. In some cases as much as 14 cc. (instead of 8 cc.) is required.

Twenty-eight children in whom complete complement fixation was secured by the use of Sauer's vaccine were exposed to whooping cough and did not contract the disease.

A vaccine twice as strong as that prepared by Sauer has been used in 100 cases without harmful effect and with the production of complement fixation more rapidly and with a smaller amount of vaccine.

MANAGEMENT OF THE RETARDED CHILD

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The parents of a retarded child have a serious problem, which merits the best thought of their physician. Many physicians have little interest in the problem and do not bring to these parents such aid as is possible. This situation is unfortunate.

It is not within the province of this article to consider the differential diagnosis of mental retardation. There is need for caution in diagnosing mental deficiency in the child who has a sensory handicap, such as deafness, a motor handicap, such as spastic paralysis, or a handicap in a special type of learning, such as reading disability. A false diagnosis of feeblemindedness is a serious mistake. A physician will be less likely to find himself in embarrassing error if he will avail himself, if possible, of the services of an adequately trained clinical psychologist in treatment of all patients with suspected mental retardation, except perhaps the grossest. Moreover, the technics of the psychologist are of value not so much because the physician is apt to diagnose mental deficiency falsely as because he is likely to pass over the milder degrees of mental retardation without adequate recognition. Even the experienced physician may find himself not infrequently mistaking verbal facility or alertness for intelligence.

The concept of mental retardation includes all degrees from dulness to idiocy. Some of the most acute problems related to mental retardation occur in children above the threshold of feeblemindedness. Manifestly the problem of the management of an idiot will be quite different from the problem of the management of a dullard. The problems of the retarded child are often involved, and only certain frequent features can be discussed in this article.

The concept of retardation is closely associated with the concept of mental age. A mental age of 5 years represents the intelligence, or intellectual capacity (not the social maturity), of the "average" 5 year old child. By definition most children attain a mental age of 5 at about 5 years of age. The exceptional child may attain it by 3. The retarded child attains it later or even not at all.

The intelligence quotient, or I. Q., is obtained by dividing the mental age, or M. A. (as indicated by the performance of an intelligence test), by the chronological age, or C. A., and multiplying the result by 100. Thus the child of 3 years and no months with a mental age of 5 years

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Studies 264, series C, from the Institute for Juvenile Research, Dr. Paul L. Schroeder, Director.

and no months has an intelligence quotient of 167. Increment in the chronological age above 15 [1] is ignored, as experiment reveals that the growth of intelligence is usually completed or approximately completed at this time.

Practical experience has shown that the intelligence quotient on an individual test, administered by an adequately trained and experienced clinical psychologist, is remarkably stable on retesting in most cases, not complicated by progressive disease of the brain or psychosis. The following classification is used at the Institute for Juvenile Research. Some indication of the occupational and educational implication is included.

Intelligence Quotient	Classification	Occupational and Educational Capacity
0– 19	Idiot	Will always require custodial care; not educable in school subjects
20– 44	Imbecile	Can learn to dress self; attend to body needs and do simple tasks like dusting; not educable in school subjects
45– 69	High grade mental defective [2]	Under favorable conditions capable of self-support in simple occupation such as labor of simplest sort; usually does not advance in school beyond the fifth grade
70– 79	Borderline defective	Capable of self-support in simple occupation such as unskilled labor; usually does not graduate from elementary school
80– 89	Dull	Semiskilled and low skilled occupation; ability adequate to complete elementary school
90–109	Average	Skilled occupation; can usually profit by two to four years of training at high school
110–119	Superior	Technical occupational level; can usually profit by two to four years of training at college
120–139	Very superior	Professional occupational level; good college ability
140–	Extremely superior	High professional level; superior ability in work at university

1. Some psychologists use 14 and some 16. Distinction should be made between the growth of intelligence and the growth of experience. The person's ability to meet intelligently the practical problems of living usually increases long past these ages, but this increase is due to growth of knowledge and experience and does not transfer to a problem so new that the knowledge and experience are without value.

2. This is the group for which Goddard coined the word moron. Since the meaning of the word has been perverted by newspaper usage, it is best avoided unless its user is certain his hearer will correctly understand it. An older and appropriate term is simpleton.

The following tabulation briefly abstracts performance and education intellectually appropriate to various mental age levels. Of course, social considerations must be recognized in planning.

Mental Age	Indication of performance or training usually possible
1 to 2 years	Walking; simple speech; some toilet training
2 to 3 years	Simple speech; simple self-help; toilet training
3 to 4 years	Simple self-help; nursery school
4 to 5 years	Self-help; nursery school
5 to 6 years	Washing dishes; sandpapering furniture; kindergarten
6 to 8 years	Mowing lawn; ironing by hand; first and second grade
10 to 12 years	Carrying mail; canning; fifth and sixth grade

When a child is recognized as mentally retarded, regardless of the degree of the retardation, the first step in treatment is usually to bring the parents to an understanding and acceptance of his handicap. It is certainly unnecessary, and nearly always unwise, to blunder into this by advising the mother or father that the child is feebleminded or an idiot. The attitude which parents commonly take toward a mental handicap is quite different from that which they take toward a physical handicap, and the discussion of the former frequently needs to be initiated with considerable adroitness. Parents of a child even grossly retarded will often insist that he is intelligent. ("He can't talk, doctor, but he's very bright. He understands everything that we say to him, and he has a wonderful memory.")

The introduction of the subject to parents with a term such as mental defective, feebleminded, idiot, imbecile or moron is unwise for two reasons. In the first place, these terms do not convey to the average parent an understanding of the nature of the handicap. They convey simply the idea that the child is mentally abnormal, and parents are likely to resent such an implication. The use of the word "moron" is particularly execrable since newspaper usage has in many localities led the public to believe it is synonymous with rapist or sex offender. In addition to the fact that these expressions do not, as a rule, convey to the parent any real understanding of the nature of the child's handicap, they are unnecessarily harsh and brutal and frequently serve merely to antagonize the parent and to keep him from accepting the diagnosis. With many parents the diagnosis, if it is to be accepted, must be conveyed gradually and in kindly, understanding terms, which to the parent do not represent an attack on the child. While there must be individualization of handling here as elsewhere, the following type of approach is usually successful:

The physician reviews with the mother the child's developmental history, specifically, in terms of age of standing, walking, speaking words, using sentences and so forth, obtaining from her comparisons with the development of other children, preferably in the family. After

the mother has gone over this, the physician may remark that the child's development has been slow. This fact is usually accepted by the parent. The physician may then remark that the child's present level of understanding and behavior is more like that of a younger child than like one of his age. This conclusion in turn is usually accepted. If at this point the mother is asked to state at what age she thinks most children display understanding and behavior like that of the patient, she may give a surprisingly accurate estimate of the child's mental age. Frequently she will somewhat overestimate the child's mental age, and the physician may find it wise to give, perhaps only tentatively, the opinion that the child is a little younger in his development than she has recognized. This approach will, in the great majority of cases, accomplish the first step, i. e., bring the parent to look at the child's present problem in terms of developmental level.

If the child's retarded development can legitimately be ascribed to an external cause, e. g., to an injury sustained at birth or to toxic encephalitis in infancy, it is usually wise to emphasize this point and thus make the retardation a symptom of physical injury, which is easier for most parents to accept than what they may view as a familial taint. Circumstances may alter this rule. If a birth injury is related to premature labor which the mother feels she brought on by foolish activity, such an emphasis is unwise, since it serves to reemphasize or to create in her a sense of guilt over the child's handicap. Also, the physician should be careful not to cast an unjust reflection on the quality of the obstetric care the mother received. Resentment toward the obstetrician may usually be avoided by some emphasis on the difficulties of delivery, the inevitable pressure on the child's head, the occurrence of cerebral injury in normal labor, etc.

Parents frequently feel a sense of responsibility, which often merges into guilt, for the handicap of a retarded child, often for an illogical or even superstitious reason. Particularly if the pregnancy was unwelcome and the mother attempted an abortion, or in some cases even considered an abortion, is this likely to be true. While it is desirable for the parents to feel responsible for their child, a deep sense of guilt over the child's handicap is essentially unhealthy and interferes with the parents' ability to train the child wisely.

It is usually wise at this point to emphasize the nature of intellectual capacity. Many parents think of intelligence as something which may be developed or sharpened by drill. Frequently they have been seeking by constant drill on nursery rhymes or school subjects to "bring the child up." The physician can point out that they have been expecting of the child a performance which would be reasonable for the average child of his age but which is distinctly beyond this child's developmental level. A homely but useful illustration is that if one has a 2 gallon

bucket one cannot get 3 gallons of water into it, no matter how long he pours. The child can learn only what his capacity permits. The parents are advised to treat the retarded child as a young child. The concept of retardation presented in this fashion carries with it an implication of the child's need for patient handling. This recognition of need for patience with the child is of kindly feeling-tone, compared with the connotation of abnormality attached to the terms feeblemindedness or mental deficiency. The second step, which may usually be accomplished by the foregoing procedure, is to bring the parent to consider the child's training in terms of that which is within reach of, and appropriate to, his level of mental development. With the lower developmental levels this training will be for control of the bowel and bladder and for speech; at levels slightly higher it will be patient encouragement in self-help, such as dressing, in the performance of simple household tasks, gardening or other manual activities, and at still higher levels, in school subjects. It is important not only that parents do not expect too much of a retarded child but also that they expect of him as much as is reasonable.

The third step of the procedure should be to bring the parents to an understanding and acceptance of the future. They may be told that extensive experience has shown that children who are mentally retarded in early childhood cannot be expected to catch up. They will, of course, grow and develop, but they will continue to develop slowly. If a reliable intelligence quotient is available, the physician may for his own information approximate the highest mental age to be expected by multiplying the intelligence quotient by 15 and pointing off 2 decimals; i. e., the ultimate expected mental age of a child with an intelligence quotient of 60 would be 9 years. In general, the amount of retardation remains proportionately the same until the completion or practical completion of mental growth at about 15 years of age, i. e., the child who at 6 has a mental age of 4 may be expected at 9 to have a mental age of about 6 and will probably never develop a mental age much beyond 10 years.

Until convinced of the permanent nature of mental retardation, parents will persistently seek a cure. If the physician even tacitly holds out hope in this direction, his action will probably be destructive.[3] Parents will grasp at a straw, and if they retain a vain hope the child can be made to "catch up" mentally, they will usually not be able intelligently and realistically to face the problem of the child's handicap. Further-

3. A large number of physicians treat retarded children with thyroid. The available evidence indicates that thyroid does not raise the intelligence even of cretin children, at least after the first two years of life. When treatment of cretins with thyroid is instituted in infancy, it may, in some cases, prevent the occurrence of retardation. When it is used in children who show no signs of cretinism, it frequently serves merely to add nervous irritability to the problems of a retarded child.

more, parents who are not brought to an acceptance of the child's retardation run from one physician or clinic to another, until they frequently fall into the hands of some charlatan, who exploits their misfortune.

At this point in the interview, even the mother who has come bristling rather belligerently with insistence that her child is bright and is simply "nervous" will usually melt down, frequently with some tears, to an acceptance of the opinion given her and be in a mood favorable for the next step of the interview, which is to aid her best to meet the child's problem. Such parents are often more than half aware of the child's retardation but are seeking to deny it to themselves and are consequently defensive. They often welcome an opportunity to talk the matter over with some one whom they feel has a sympathetic attitude. The suggestions given must depend on the degree of mental retardation.

Parents of an idiot are apt to feel, and express their feelings, that the child's handicap is a tragedy. Their feelings may interfere with the proper training of the child within his capacity to learn. It is sometimes of value to point out that the child is, after all, not unhappy (few idiots are), that from the child's point of view he is not unfortunate and that he will always be well cared for and to explain to the parents that they are really grieving not over the child but over the disappointment of their own ambitions and expectations, i.e., that the parents are being sorry not for the child but for themselves. At this time or later it may be pointed out to the parents of an extremely retarded child that he will always require care and that probably they will not be able to extend that care throughout the child's life, i. e., that ultimately the question of placement in an institution, private or public, will have to be faced.

Many parents conceive of an institution as a place for the cure of feeblemindedness; they should be brought to realize that the care is for the more severely retarded child merely custodial. The mere fact that a child is feebleminded is no reason for placement in a public institution. If the parents are unable or unwilling to care for the child adequately at home, if the child's care is an unreasonable burden on the mother, or one to which her health is not equal, if the child's presence in the home is manifesting an unfavorable influence on other, normal children or if the child can be considered a menace in the community, institutional placement should be advised. Otherwise, there is no reason to encourage parents to transfer the responsibility for the care of a retarded child, but there is some value in their realizing the possible ultimate need for commitment and the availability of institutional care if it is needed. Some parents have unjustified horror of institutions and before considering such placement may need to visit the institution, in order that they may learn its character at first hand.

With a less severely retarded child of 6 or 7 years, placement in the first grade may be postponed until it appears that the child's mental capacity is equal to what is expected in this class. The program of the kindergarten is, of course, much more flexible and less exacting of the intelligence than that of the first grade. With the older child who is at school, parents need to be brought to an understanding that he must be permitted to take school at the tempo of his ability, that he must be expected to repeat some grades and that it is unwise to criticize him for failures or to lay stress on school achievement, since such practices can only bring unhappiness. The concept of the child's retarded mental development needs repeatedly to be brought up, in order to offset the parents' natural tendency to expect too much. It is not necessary to ram a particular mental age down the throats of the parents, but it is important that they obtain an understanding of the child's approximate level of intellectual maturity. The compensatory tendency on the part of the parents to try to make up for a child's slowness with excessive drill or excessive pressure is particularly noticeable with children not feebleminded but simply dull who have the misfortune to be born in families of a high intellectual, cultural and educational standard.

Some of the parental effort at compensation may be advantageously and usefully canalized. If the degree of retardation is not too severe, it may be emphasized to parents that while the child's academic possibilities are limited, he may be able to develop some skill with his hands in activities which do not make great demand on the intelligence. If some of the excessive parental solicitude can be metamorphosed to sufficiently patient encouragement and aid in the development of such skills, the child may have a happier childhood and become a self-supporting, if not entirely adequate, adult. The retarded child usually stands in particular need of encouragement and of a sense of acceptance.

The training of a retarded child is particularly difficult for several reasons. It is difficult for parents to determine what is reasonable to expect of him. Most parents have some conception of what is reasonable to expect of a 4 year old or a 6 year old, but in order to gain a conception of what is reasonable to expect of a retarded child, they must ignore the surface implications of his physical size and chronological age. He cannot be measured by the standards of other children. Because parents in general do not adequately realize this, they commonly expect of the retarded child a standard of performance beyond his ability. Parents again, the mother in particular, usually think of a retarded child of their own with a rather high degree of sympathy or pity and with the feeling, which has some justification, that this child needs extra protection. The dependency of the handicapped child often overstimulates parental protectiveness, and intelligent parents often find it difficult to require of the child that of which he is capable or to avoid

giving in to his every whim. It is, in other words, difficult for parents to avoid spoiling the retarded child. Such spoiling is extremely common and not infrequently creates a more serious obstacle to adjustment than the retardation itself. Most parents are capable of giving some intelligent response to a warning against such spoiling, if it is pointed out to them how natural this tendency is and yet to what unhappiness it leads, since it adds still another handicap to the one already existing. With a milder degree of retardation, which the parent may not recognize, an alternative attitude of impatience with the child's shortcomings may need to be modified by some kindly interpretation of the child's limitations, such as has already been discussed.

Parents in good economic circumstances may be advised to place a retarded child in one of the private schools for children so handicapped. The child is freed from unequal competition with normal children and may be given simple training, suitable to his ability. Parents who cannot afford such placement are often eager to attempt it in the hope that their child will be cured in a year or two. They should be discouraged from unreasonable sacrifice of the opportunities of their normal children for the sake of providing special opportunities for a child so little able to profit by them.

Institutional care and training are too expensive to be a general solution for the problem of training children with the milder degrees of mental retardation. It is necessary that some special provision be made for training such children in the community. Many urban school systems have taken cognizance of this need by providing special ungraded rooms or even special schools, where more or less effort is directed to providing a curriculum suitable for the education of these handicapped children. Such a program should include some extra emphasis on drill in simple fundamentals, a liberal addition of training in handwork and simple craftsmanship and opportunity for cooperative projects or activities to further the child's social development. Unfortunately the ungraded room is likely to become known among the school children as the "dummy room," or some equivalent expression, and to have social disadvantages. Intelligent educators will be alert to minimize the disadvantages, and for most retarded children the disadvantages will be distinctly less than those of the alternative of placement in a regular grade.

The social adjustment of the retarded child is difficult but extremely important. Parents who expect too much of him are likely at the same time to overrestrict his social contacts with other children. In general, the retarded child will spontaneously gravitate toward association with children somewhat younger than he. Because of his inferior understanding, his retardation at school and perhaps evident simpleness, he is apt to become the object of teasing or to be used like the ass as a

symbol of stupidity. When the play of the child is under the supervision of an adult, these developments may be discouraged.

As the retarded child approaches adolescence, parents need to be cautioned concerning the protection and training necessary. The retarded adolescent girl, with her mental immaturity, poor judgment and suggestibility, needs careful parental supervision to make certain that no one takes undue advantage of her simpleness. The retarded adolescent boy needs the background of good home training to keep him from childlike collision with social taboos. The parents are often overapprehensive about the likelihood that their retarded child will commit sex crimes at adolescence or later. As stated earlier, the newspaper interpretation of the word moron is largely responsible for this attitude. If it is explained to them that the retarded adolescent boy usually has normal sex drives but simply lacks adequate judgment and that they can protect him from falling into serious error simply by supplying training, by teaching him to respect conventional taboos, they will often be much relieved. Of course there are instances in which even good training fails, but these are exceptional.

The child who is mentally retarded by reason of injury sustained at birth or of encephalitis in infancy is particularly prone to be of a restless, distractible, excitable nature. These characteristics may wisely be interpreted to the parents as a part of the child's handicap. Such a child needs special protection from too much excitement. Calm, patient management is particularly important. Frequent change of occupation or activity is necessary in his training to keep his interest. An effort to force sustained attention to the task in hand will usually be harmful, rather than beneficial. Care needs to be exercised to prevent overfatigue.

The physician who is willing to give his best thought and effort to the problems faced by the parents of retarded children and to consult with them at intervals, which as a rule need not be frequent, will earn their gratitude and may at the same time add to his means of livelihood. There is literature available to aid him in this work.[4]

4. The following references are particularly useful: Tredgold, A. F.: Mental Deficiency, ed. 5, New York, William Wood & Company, 1929. Wallin, J. E. Wallace: The Education of Handicapped Children, New York, Houghton Mifflin Company, 1934. Penrose, Lionel S.: Mental Defect, London, Farrar & Rinehart, Inc., 1934. Schroeder, Paul, and Bartelme, Phyllis: A Mental Health Program as a Juvenile Court Method of Supervising the Feebleminded, Proc. Am. A. Study of Feebleminded **52**:37, 1928. Schroeder, Paul: Behavior Difficulties in Children Associated with the Results of Birth Trauma, J. A. M. A. **92**:100 (Jan. 12) 1929. Fischel, Marguerite K.: The Spastic Child, St. Louis, C. V. Mosby Company, 1934. Svendsen, Margaret, and Schlotter, Bertha: An Experiment in Recreation with the Mentally Retarded, Behavior Research Fund Publications, Department of Public Welfare, Springfield, Ill., 1932. Beaman, Florence N.: The Value of Social Factors in the Training of the Defective Child, Am. J. Sociol. **37**:240, 1931.

OTOGENIC SUPPURATIVE PAROTITIS IN CHILDREN

REPORT OF FIVE CASES

JOHN M. ADAMS, M.D.

MINNEAPOLIS

The syndrome of which the condition in the five cases reported in this paper are typical is characterized by preceding acute otitis media with suppuration. Concomitantly with the discharge from the ear, pain appears just anterior to the external auditory meatus. Early in the course there is pain on moving the jaw, and the temperature rises abruptly (to from 103 to 105 F.). The swelling in the affected area appears early, rapidly increases in size and is associated with edema and tenderness. The edema extends to the orbit, above the zygoma, and occasionally around the auricle to involve the mastoid region. The pain is acute. Fluctuation is elicited with difficulty, appearing late. In four cases the area was incised and drained, with prompt relief; in the fifth case the abscess ruptured into the external auditory canal and drained watery purulent material, with marked relief to the patient.

ANATOMY

It has been clearly shown that the glenoid lobe of the parotid gland is intimately associated with the auricular area, as is the articulation of the mandible [1] (fig. 1).

The location of the glenoid lobe was further described by Muller [2] as follows: "A prolongation behind the articulation of the lower jaw into the posterior portion of the glenoid cavity immediately in front of the external auditory canal, is called the glenoid lobe" (fig. 2).

Deaver [3] gave a complete description of this region and brought out the important point that the fibrous envelop of the parotid is incomplete above and in front, making it possible for pus to extend into the pterygomaxillary space and temporal fossa. With reference to the relation of the parotid gland and the temporomaxillary articulation, he stated that in inflammation of the glands movement of the articulation is attended

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From the Abbott Hospital and the Janney Children's Hospital.

1. Spalteholz, Werner: Atlas of Human Anatomy, ed. 4, Philadelphia, J. B. Lippincott Company, 1924, p. 52.

2. Muller, George P., in Davis, G. G.: Applied Anatomy, Philadelphia, J. B. Lippincott Company, 1924, p. 52.

3. Deaver, John B.: Surgical Anatomy, Philadelphia, P. Blakiston's Son & Co., 1901, p. 520 and 521.

by pain; the extent to which the lower jaw can be depressed under the circumstances is dependent on the amount of swelling. He added: "The intimate relation existing between the parotid gland, the external auditory meatus, and the temporo-maxillary articulation is to be borne in mind, as a parotid abscess may open into the meatus or cause involvement of the joint."

A further significant point relative to this region was made by Talbot.[4]

The posterior extremity of the glandular (parotid) substance is in direct apposition with the cartilaginous portion of the external auditory canal, its fibrous capsule the only separation. This part of the canal presents a deficiency in cartilage, its place being taken by a fibrous membrane; as a result there are two or

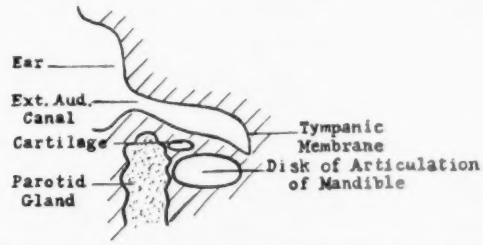

Fig. 1.—Drawing of cross-section showing anatomic relation of the parotid gland, auricular area and articulation of the mandible.

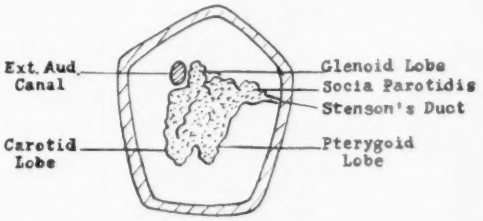

Fig. 2.—Drawing showing position of the glenoid lobe of the parotid gland.

three deep fissures running vertically through the cartilaginous wall (incisurae santorini). In acute suppurative parotitis pus may burrow through these relatively less resistant parts of the wall, and discharge through the ear.

Talbot [4] stated that infection by way of the lymphatics may occur, but this presupposes an infective focus within the lymphatic radius of the parotid gland. Piersol [5] affirmed:

The parotid nodes, lying in and upon the gland, receive lymph from and consequently may be infected by lesions of the scalp, . . . external auditory meatus, the tympanum, or temporo-mandibular joint. Suppurative inflammation

4. Talbot, H. S.: Acute Suppurative Parotitis, Am. J. Surg. **25**:267, 1934.
5. Piersol, George A.: Human Anatomy, Philadelphia, J. B. Lippincott Company, 1907, p. 955.

of these deeper nodes gives rise to a true parotid abscess, which on account of the resistance of the strong parotid fascia, will be under great tension.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis presents a problem to the pediatrician as well as to the otologist. The condition has been confused with epidemic parotitis, as it was in one of the cases reported here. The inflammation does not usually involve the whole gland; the maximum point of swelling is higher and directly anterior to the ear, extension being upward rather than downward. The disease is unilateral, and unless attacked early the swelling may last more than ten days.

The question of zygomatic mastoiditis was a real one, but in no instance was it possible to demonstrate involvement of this region by roentgen examination or by exploration. The fact that edema and tenderness may extend behind the auricle to involve the mastoid region as well serves to increase the difficulty of diagnosis. In one instance (case 4) there were definite mastoiditis and lateral sinusitis, with mural thrombosis to complicate the picture.

The information to be had in the literature regarding this syndrome is scarce. I was unable to find a reference to the complication in the standard textbooks. A closely associated (if not identical condition) is described in the literature under the title of "Pterygomaxillary Abscess Associated with Otitis Media."[6] The difficulty in opening the mouth and associated pain appeared early in the cases reported here (cases 1, 2 and 4). Greenfield[6a] stated: "There is some difficulty in opening the mouth, but this symptom does not become pronounced until later in the disease." He also maintained that "when the edema is at its maximum careful examination reveals the fact that the edema stops short of the zygoma." It was definitely felt in cases 1, 2, 3 and 4 that edema extended over and above the zygoma. Referring again to Deaver's description, "In parotid abscess the pus may on account of this gap in the fascial envelope, extend into the pterygo-maxillary region and by way of the latter into the temporal fossa." Greenfield[6a] also stated: "There is temperature varying between 99 and 103." In cases 2, 3 and 4 of this series the temperature was recorded as 105 F. or more at the height of the illness. In case 4 the temperature was recorded as 107 F. at one time.

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6. (*a*) Greenfield, Samuel D.: Pterygomaxillary Abscess Associated with Acute Suppurative Otitis Media Simulating Zygomatic Mastoiditis, Laryngoscope **44**:232 (March) 1934. (*b*) Grant, C. C.: Abscess of the Pterygomaxillary Fossa Complicating Otitic Infections, Arch. Otolaryng. **16**:845 (Dec.) 1932. (*c*) Strauss, J. F.: Pterygomaxillary Abscess Complicating Acute Mastoiditis, Ann. Otol., Rhin. & Laryng. **36**:477 (June) 1912. (*d*) McKenzie, D.: Otitic Pterygomaxillary Abscess Induced by Thrombophlebitis of the Jugular Bulb, Proc. Roy. Soc. Med. (Sect. Laryng.) **16**:53 (Aug.) 1923.

The clinical course in acute suppurative parotitis as described by Talbot [4] was typical in these cases. He stated that the onset is most often sudden, with fever, pain and swelling over the gland. The pain may be extreme, and extensive edema of the surrounding soft parts may be so marked as to result in closure of the eye on the affected side. Motion of the lower jaw is painful and difficult. The initial temperature may vary from 102 to 105 F.

Grant [6b] found reports of four cases of abscess of the pterygomaxillary space in the literature, in two of which the condition was associated with otitic infections.[6c, d]

Peroni [7] reported in the Italian literature in 1934 two cases of abscess of the parotid gland of otogenic origin, both in adults. He stated that parotitis may be secondary to infections within the region of the gland and included mastoiditis and otitis media as etiologic factors. Inflammation of the middle ear may involve the preauricular nodes and extend by way of these to involve the parotid gland.

REPORT OF CASES

CASE 1.—B. B., aged 10 years, was admitted to the hospital on Oct. 24, 1935, and discharged on October 30. The chief complaint was swelling on the right side of the face, of two weeks' duration. The past history was not significant.

Two weeks prior to admission a small painful swelling was noted just anterior to the right ear. Severe pain on opening the mouth was present. Two or three days after the onset the right ear began to discharge. The patient was seen by his physician, and the condition was treated as epidemic parotitis. The temperature was elevated throughout (the degree was unknown). After ten days during which the swelling and temperature persisted the patient was thought to have an abscess. Hot packs were applied until his admission to the hospital on the fourteenth day.

The temperature on admission was 101 F. There was a large indurated, painful swelling over the right side of the face, extending from well above the zygoma to the border of the mandible, with the maximum point just anterior to the right ear. The mass was not red and hot, but it was tender and fluctuation was difficult to elicit. The patient was unable to speak clearly, and limitation of motion of the mandible was evident. The right ear drum was bulging, and there was purulent exudate in the external auditory canal.

Laboratory examination showed that the urine was normal.

Roentgen examination revealed cloudiness of the right mastoid cells; there was no evidence of destruction, and the zygomatic region was normal.

On October 25, with the patient under ethylene anesthesia, a linear incision was made anterior to the right ear. Below the fascia of the parotid a large amount (from 2 to 3 ounces [56.7 to 85 Gm.]) of pus and necrotic material was obtained. The temperature fell to normal eight hours postoperatively and remained there throughout the patient's stay in the hospital.

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7. Peroni, A.: Ascessi della loggia parotides di origine otogena, Arch. ital. di otol. **46**:447, 1934.

One month after his discharge the patient was clinically well. The wound over the parotid was healed, and there was no discharge from the ear.

The final diagnosis was: (1) acute suppurative parotitis on the right, and (2) otitis media on the right.

CASE 2.—J. T., aged 9 years, was admitted to the hospital on Nov. 13, 1935, and discharged on November 21. The chief complaint was earache, of three days' duration. The patient had had an infection of the upper respiratory tract, with cough, for three weeks.

The present illness began three days prior to admission, when the patient complained of bilateral earache, with moderate deafness. On his admission for myringotomy (which had been advised twenty hours earlier) the temperature was 99 F. Both ear drums were inflamed, and the landmarks were obliterated. The tonsils were large and swollen, with white exudate in the crypts. Otherwise, examination gave negative results.

On myringotomy, with the patient under ethylene anesthesia, purulent material was obtained from both sides, cultures of which yielded hemolytic streptococci and staphylococci. Four hours postoperatively the temperature had risen to 105 F. Eight hours later it was still 105 F., and the patient complained of acute pain anterior to the right ear. Pain referred to the right mandibular articulation made opening the mouth difficult. This area was extremely tender on palpation. Both ears were draining profusely. Eight hours after the onset of the pain, swelling was noted in the preauricular region.

Examination of the urine revealed a trace of albumin and from 20 to 30 white blood cells per low power field, uncentrifugated.

On November 15 swelling was definite over the area of the parotid gland (glenoid lobe), and the patient was unable to open her mouth. The edema had spread to involve the area about the zygoma, extending over it and posteriorly to the mastoid area. There was no swelling below the mandible. On November 16 roentgenograms of the mastoids showed them to be of the mixed cell type. The left mastoid was comparatively normal; the right showed some haziness about the midportion but no abscess formation.

On November 17 the swelling was marked. There was edema of the right orbital area, and elevation of temperature persisted. Drainage from the right ear was greatly increased, the material being of watery consistency.

On November 18 profuse watery drainage, which was increased by pressure over the parotid, continued. The swelling decreased, and the temperature fell to 100 F. On November 21 the patient was discharged, with a small amount of swelling over the parotid. The left ear had cleared up entirely, while the right canal still drained profusely.

Follow-up examination, December 10, showed that the patient was well. Following her discharge from the hospital the drainage ceased, and the parotid became moderately swollen. She experienced an increased flow of saliva, and the swelling receded. This recurred several times, the flow of saliva being less in amount each time.

The final diagnosis was: (1) bilateral otitis media and (2) acute parotitis on the right.

CASE 3.—R. S., aged 8 years, was admitted to the hospital on Aug. 8, 1935, and discharged on September 10. The chief complaint was pain in the left ear, of one week's duration. The past history was not significant.

One week prior to admission the patient complained of pain in the left ear. The ear drum was opened three days later, and pus was obtained. The temperature continued to be elevated while the patient was at home. On admission the

temperature was 104.8 F. The patient appeared to be acutely ill. The throat was red, and the tonsils were large and swollen. The left ear was draining thick purulent material. The right ear drum appeared to be red and bulging. Examination of the urine showed a trace of albumin. On August 17 the hemoglobin content was 63 per cent (Sahli), and the white cell count of the blood was 28,800.

The day after admission the patient complained of pain and tenderness anterior to the left ear. A slight swelling was noted over the preauricular area. There were pain and difficulty in opening the mouth. The swelling continued to increase, and the patient complained of intense pain.

On August 13 the right ear was discharging, and the temperature was 104.8 F. A small incision was made anterior to the left ear, and below the parotid fascia thick purulent material was obtained. The pain was markedly relieved. The temperature remained elevated, however. On August 19 the patient was given a direct transfusion. Roentgenograms of the mastoids revealed both mastoids to be of the small cell type; there was evidence of involvement on both sides but no destruction was present.

On August 20 bilateral mastoidectomy was done. The operative note read: "The mastoids were found to be very sclerotic but were cellular about the antrum and retrofacial areas. Granulations were curetted out, and the opening to the antrum was enlarged."

On August 22 the temperature continued to be elevated. The swelling extended over the zygoma and well anterior on the face, involving the left orbit. On August 23 the incision anterior to the ear was enlarged and better drainage established. On August 27 the swelling was much smaller, and the temperature reached normal. Convalescence was slow, but the patient was discharged on September 10, markedly improved.

Follow-up examination, one month after discharge, showed that all the wounds were healed, and the patient appeared to be in good health.

The final diagnosis was: (1) bilateral otitis media, (2) bilateral mastoiditis, and (3) parotid abscess on the left.

Case 4.—W. S., aged 7 years, was admitted to the hospital on April 17, 1935, and discharged on June 3. The chief complaint was drainage from the right ear since April 8 and swelling of the right cheek since April 10. The past history was irrelevant.

Suppurative otitis media developed on April 8. On April 10 the temperature was noted to be 104 F. On April 11 the patient fell part way out of bed, striking the right side of his face on a chair. On April 12 he complained of pain over the parotid area, and a moderate swelling was noted, with pain and difficulty in opening the mouth.

On admission the temperature was 103.6 F. The right side of the face was swollen and tender. The patient was unable to open his mouth more than ½ inch (1.27 cm.). There was a profuse purulent discharge from the right ear. The left ear drum was normal. Otherwise, examination gave negative results. Roentgen examination of the skull and the cervical part of the spine showed no abnormalities. On April 18 the swelling had increased, and the patient was unable to open his mouth. The right mastoid was draining profusely. The patient had two chills, and the temperature rose to 107 F. On April 19 roentgen examination revealed localized destruction in the midportion of the right mastoid. Culture of the blood on April 20 showed long chain, gram-positive streptococci. On April 21 the temperature was 105 F., and the patient had a chill. The jugular vein was ligated on the right. A submandibular incision was made

and a forceps plunged through the parotid capsule. A teaspoonful of yellow pus was evacuated. The mastoid was opened and found to be broken down; the sinus was explored and packed off. Culture of material from the parotid revealed streptococci.

The temperature gradually fell to normal, and the suppuration decreased in amount. On April 27 torticollis was noted on the left. On May 25 the torticollis was much improved. The drainage from the wound in the mastoid was slight. On June 3 the patient was discharged well.

The final diagnosis was: (1) bilateral otitis media, (2) mastoiditis on the right, (3) mural thrombosis in the lateral sinus and (4) abscess of the parotid gland on the right.

CASE 5.—J. N., aged 13 months, was admitted to the hospital on May 21, 1935, and discharged on June 9. The chief complaint was swelling of the right side of the face, of two days' duration.

On April 15, one month prior to admission, a nasal discharge developed. On May 2 the patient began to cough, and his temperature was elevated. He was taken to another hospital on May 7, where he was found to have bilateral bronchopneumonia. On May 10 both ear drums were opened; they had discharged purulent material since. On May 19 swelling in the preauricular region on the right side developed. The patient was transferred to the Abbott Hospital on May 21.

On admission the temperature was 103.8 F. There was a swelling over the right side of the face, which was maximal in the preauricular region. The right ear was draining profusely and the left slightly. There was a thick purulent nasal discharge. A large hard cervical node was present on the right side. Otherwise, the results of examination were negative. Examination of the urine gave negative results.

The patient continued to have an elevation of temperature, and on May 25 an incision was made anterior to the right ear. Below the parotid fascia thick purulent material was obtained.

On May 27 the temperature fell to normal, and except for one rise to 101.6 F. it remained normal throughout the course. Nasal discharge and drainage from both ears persisted until the patient's discharge, at which time it was very slight.

On follow-up examination, six months after discharge, the patient was reported to be well.

The final diagnosis was: (1) bilateral otitis media, (2) sinusitis and (3) parotid abscess on the right.

SUMMARY

In four of the cases there was preceding otitis media, with a purulent discharge at the time of the onset of the parotitis. In the other case a discharge from the middle ear developed soon after the onset of the inflammation of the parotid.

The onset of the parotitis was sudden and was followed by preauricular swelling, widespread edema, intense pain and pain on opening the mouth.

The temperature was 105 F. or above in three of the cases. There were varying degrees of mastoiditis, as demonstrated by the roentgen rays. In one case there was definite destruction.

A parotid abscess was drained surgically in four of the cases, and in one spontaneous rupture into the external auditory canal took place.

CONCLUSIONS

In these cases acute suppurative parotitis complicated otitis media. The problem of mastoiditis or zygomatic mastoiditis was seriously considered, and it was also necessary to rule out epidemic parotitis. The clinical picture was typical of acute suppurative parotitis. The location of the deep preauricular or parotid lymph glands draining the auricular area pointed to these as the route of infection of the parotid gland. The anatomic relationship explains the involvement of the mandibular joint and the mode of spontaneous rupture of the abscess into the external auditory canal.

ERYTHROCYTES AND HEMOGLOBIN OF THE BLOOD IN INFANCY AND IN CHILDHOOD

I. SIZE AND HEMOGLOBIN CONTENT OF THE ERYTHROCYTES IN NUTRITIONAL ANEMIA

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CINCINNATI

The term nutritional anemia designates a type of anemia especially prevalent among infants of 1 and 2 years, currently thought to be due mainly to lack of iron, which, derived either from stores in the body or from food, is needed for building hemoglobin. The severe form of the disease is seen most frequently among infants who have too long been given an exclusive milk diet, but it is seen also among infants who have been offered a seemingly well balanced diet. In most instances the anemia tends to improve spontaneously, as a rule coincidentally with the increasing acceptance of a well balanced diet, but even in infants who recover spontaneously (i. e., without iron medication) the period of transitory anemia is a critical one, in which the hazards of intercurrent infection and general nutritional disturbances are increased. The evidence produced by recent investigations [1] that there is a higher morbidity among anemic infants than among nonanemic infants emphasizes as a major pediatric problem the need for increased prevention of the condition as well as for better aids to its early diagnosis and cure.

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A preliminary report of these studies was read at a meeting of the American Pediatric Society at Asheville, N. C., May 5, 1934.

1. (*a*) Mackay, H. M. M.: Nutritional Anaemia in Infancy, with Special Reference to Iron Deficiency, Medical Research Council, Special Report Series, no. 157, London, His Majesty's Stationery Office, 1931; (*b*) The Normal Haemoglobin Level During the First Year of Life: Revised Figures, Arch. Dis. Childhood **8**:221, 1933; (*c*) Factors Causing Variation in the Haemoglobin Level with Age in the First Year of Life, ibid. **8**:251, 1933. (*d*) Usher, S. J.; MacDermot, P. N., and Lozinski, E.: Prophylaxis of Simple Anemia in Infancy with Iron and Copper: Effect of Hemoglobin, Weight and Resistance to Infection, Am. J. Dis. Child. **49**:642 (March) 1935.

Several extensive investigations of the hemoglobin content of the blood of normal infants, the results of which have been published during the past few years, have emphasized the fact that nutritional anemia is more prevalent than is generally recognized. Mackay [1a] examined 4,811 samples of blood from infants of the poorer classes of London and reported that at 12 months of age 42 per cent of the breast-fed infants and 70 per cent of the artificially fed infants were definitely anemic. At Madison, Wis., Elvehjem, Peterson and Mendenhall [2] reported the results of a determination of the hemoglobin content of 2,000 samples of blood from 740 children ranging in age from birth to 5 years. Approximately 38 per cent of the children at 1 year of age had less than 11 Gm. of hemoglobin per hundred cubic centimeters of blood, and approximately 10 per cent had less than 10 Gm. The range of values between 10 and 11 Gm. constitutes a borderline zone for clinically recognizable anemia in infants of that age group. Most pediatricians recognize anemia in infants whose hemoglobin content is less than 10 Gm., but among infants who have between 10 and 11 Gm. anemia often goes unrecognized or is considered clinically insignificant. The hemoglobin level of the blood considered alone is, however, a less exact criterion of anemia in such infants than the alteration of the size and the hemoglobin content of the red cells, to which attention is mainly directed in this paper.

The size and the coloration (i. e., hemoglobin content) of the red blood cells have been used as the basis for a classification of the anemias by a number of investigators. In a recent paper by Haden [3] such a classification is concisely summarized under a terminology which is employed by a number of writers at the present time, describing the red cells by terms designating normal, low or high values for their size and coloration, as follows: (1) normocytic, normochromic; (2) normocytic, hypochromic; (3) macrocytic, hyperchromic; (4) macrocytic, normochromic; (5) macrocytic, hypochromic; (6) microcytic, hypochromic. In ordinary microscopic study of stained blood films from anemic infants and children, microcytosis and hypochromia are commonly noted, but quantitative measurement of these characteristics is necessary for an accurate description of the cells. Although abundant quantitative data from studies of the red blood cells of adults are now

2. Elvehjem, C. A.; Peterson, W. H., and Mendenhall, D. R.: Hemoglobin Content of the Blood of Infants, Am. J. Dis. Child. **46**:105 (July) 1933.

3. Haden, R. L.: Classification and Differential Diagnosis of the Anemias, J. A. M. A. **104**:706 (March 2) 1935.

available, reported extensively by Haden,[4] Wintrobe,[5] Osgood and Haskins [6] and others, such data from the study of the blood of infants and children are comparatively scant. Haden and Neff [7] in 1924 reported studies of the red cells of eleven infants aged from 11 hours to 24 days. More recently Wintrobe [8] reported studies of the size and the hemoglobin content of the cells of fetal blood and the blood of new-born infants, and Osgood and Baker [9] reported similar studies of blood from 215 children aged from 4 to 13 years.

In the Children's Hospital Research Foundation, studies of the erythrocytes of children have been in progress during the past four years, during which time more than 500 samples of blood from normal and anemic children ranging in age from birth to 5 years have been examined. The examples described in this paper were selected for the purpose of demonstrating the characteristic changes of the red blood cells which occur during the development of and recovery from nutritional anemia. A more detailed statistical analysis of the accumulated data will be reported later.

METHOD AND TERMINOLOGY

The terminology employed in the investigation is presented in table 1, in which are listed the values determined and calculated for a sample of blood from a normal 3 year old child.

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4. Haden, R. L.: Clinical Significance of Volume and Hemoglobin Content of the Red Blood Cell, Arch. Int. Med. **49**:1032 (June) 1932; The Technique of Determinations of the Relative Mass, the Individual Cell Volume and the Volume Index of the Erythrocytes of Man, J. Lab. & Clin. Med. **15**:736, 1930; The Volume and Hemoglobin Content of the Erythrocytes in Health and Disease, Folia haemat. **31**:113, 1924-1925.

5. Wintrobe, M. M.: Anemia: Classification and Treatment on the Basis of Differences in the Average Volume and Hemoglobin Content of the Red Corpuscles, Arch. Int. Med. **54**:256 (Aug.) 1934 (correction, ibid. **54**:830, 1934); Direct Calculation of Volume and Hemoglobin Content of Erythrocyte: Comparison with Color Index, Volume Index and Saturation Index Determinations, Am. J. Clin. Path. **1**:147, 1931; The Erythrocyte in Man, Medicine **9**:195, 1930.

6. Osgood, E. E.; Haskins, H. D., and Trotman, F. E.: The Value of Accurately Determined Color, Volume and Saturation Indexes in Anemias, J. Lab. & Clin. Med. **17**:859, 1932.

7. Haden, R. L., and Neff, F. C.: The Volume Index and Color Index of the Red Blood Corpuscles in New-Born Infants, Am. J. Dis. Child. **28**:458 (Oct.) 1924.

8. Wintrobe, M. M.: Comparison of Hematopoiesis in the Fetus and During Recovery from Pernicious Anemia, Together with a Consideration of the Relationship of Fetal Hematopoiesis to Macrocytic Anemia of Pregnancy and Anemia in Infants, J. Clin. Investigation **14**:837, 1935.

9. Osgood, E. E., and Baker, R. L.: Erythrocyte, Hemoglobin, Cell Volume and Color, Volume and Saturation Index Standards for Normal Children of School Age, Am. J. Dis. Child. **50**:343 (Aug.) 1935.

In all cases blood was drawn from a superficial vein into a dry glass syringe, mixed with heparin (1 mg. of heparin to approximately 2 cc. of blood) in a small glass vial and carried to the laboratory for immediate examination. Three determinations were made (table 1): (*a*) the red cell count, expressed in millions per cubic millimeter of blood and made with a hemocytometer of the usual type, certified by the Bureau of Standards; (*b*) the volume of packed red cells, expressed in percentage of the whole blood and determined by the method of Guest and Siler,[10] in which a pair of capillary glass tubes are partly filled with blood, sealed and centrifugated for five minutes at a speed of 15,000 revolutions per minute and the columns of packed cells and plasma are measured by means of a measuring microscope; (*c*) the hemoglobin content, expressed as grams per hundred cubic centimeters of whole blood and determined by the Palmer carbon monoxide hemoglobin method,[11] modified by using a Wratten filter no. 74 over the eyepiece of the colorimeter. The hemoglobin standard for the colorimetry was checked by the Van Slyke-Hiller carbon monoxide capacity manometric method.[12] From the three values thus determined, three further values, describing the characteristics of the cells, were calculated, viz.: the mean cell volume, expressed in cubic microns

TABLE 1.—*Data on Blood of a Normal 3 Year Old Child*

Values determined for whole blood	
(a) Red cell count, millions per cu. mm.	4.55
(b) Volume of packed red cells, per cent	39.4
(c) Hemoglobin, Gm. per 100 cc.	13.4
Values calculated for red cells	
Mean cell volume ($b \times 10 \div a$), cubic microns	86.5
Hemoglobin concentration ($c \div b \times 100$), Gm. per 100 cc.	34.0
Mean hemoglobin content per cell ($c \times 10 \div a$), micromicrograms	29.5

and obtained by dividing the figure for the volume of cells in 1 liter of blood ($b \times 10$) by that for the cell count, in millions (a); the hemoglobin concentration, in grams per hundred cubic centimeters of packed cells, obtained by dividing the value for grams of hemoglobin per hundred cubic centimeters of whole blood (c) by the volume of cells (b) multiplied by 100; the mean hemoglobin content per cell, in micromicrograms, obtained by dividing the figure for grams of hemoglobin per liter of whole blood ($c \times 10$) by that of the cell count in millions per cubic millimeter (a).

The advantage of expressing the hemoglobin concentration in an absolute unit per volume (i. e., grams per hundred cubic centimeters) has been pointed out by many investigators, but this point deserves reemphasis as long as the older terminology, the expression of the hemoglobin value in percentage of an assumed normal standard, persists

10. Guest, G. M., and Siler, V. E.: Centrifuge Method for the Determination of the Volume of Cells in Blood, J. Lab. & Clin. Med. **19**:757, 1934.

11. Palmer, W. W.: The Colorimetric Determination of Hemoglobin, J. Biol. Chem. **33**:119, 1918.

12. Van Slyke, D. D., and Hiller, A.: Gasometric Determination of Hemoglobin by the Carbon Monoxide Capacity Method, J. Biol. Chem. **78**:807, 1928; Gasometric Control of Standard Solutions for the Palmer Hemoglobin Method, ibid. **84**:211, 1929.

in popular usage. The older terminology has resulted in enormous confusion in medical literature because of the adoption of a different value for the so-called normal in different parts of the world. There is no more justification for expressing the hemoglobin concentration in "percentage of normal" than for a similar expression of values for sugar, nonprotein nitrogen, calcium or other chemical constituents of the blood. The expression of the hemoglobin concentration in percentage of normal is especially unfortunate when one is dealing with infants and children, in whom the values within the recognized limits of normal variation are constantly changing with the age of the child. The term color index has a double disadvantage in this respect, as it is calculated by referring two determined values (i. e., cell count and hemoglobin content) to an assumed normal standard and then expressing their quotient as an index.

TABLE 2.—*Data on Blood from the Umbilical Cord of New-Born Infants*

	Red Blood Cells			Hemoglobin		
Blood Samples	Count, Millions per Cu. Mm.	Volume of Cells in Whole Blood, Percentage	Mean Cell Volume, Cubic Microns	In Whole Blood, Gm. per 100 Cc.	In Red Cells, Gm. per 100 Cc.	Mean Hemoglobin Content per Red Cell, Micromicrograms
1	5.93	69.1	117	22.0	31.8	37.0
2	4.80	58.9	123	19.6	33.3	40.8
3	4.99	54.3	109	19.1	35.2	38.3
4	4.23	50.6	120	17.9	35.4	42.4
5	5.05	51.5	102	17.9	34.7	35.4
6	5.07	46.1	91	16.2	35.2	32.0
7	4.02	48.4	120	15.8	32.7	39.4
8	4.10	42.9	105	13.1	30.5	32.0

The expression of the mean hemoglobin content per cell, in micromicrograms, gives a more accurate evaluation of the character of the cells which we attempt to describe under the expression color index.

OBSERVATIONS

The characteristics of the blood of new-born infants are illustrated by the data in table 2, obtained from samples of blood taken from the umbilical cord of eight infants immediately after birth. The blood of the new-born infant is characterized by a high hemoglobin content and a moderately high cell count. The latter is not, however, as high as has been generally reported in older medical literature on the subject. The cells are predominantly macrocytic and normochromic or slightly hypochromic, i. e., with a hemoglobin concentration of from 30 to 35 Gm. per hundred cubic centimeters of packed cells.

In table 3 are listed data on samples of blood taken from six infants with nutritional anemia of varying severity. The examples selected for presentation here were representative of more than fifty similar samples which were studied in the manner previously described. According to

our experience in this clinic, nutritional anemia is seen most frequently in infants between 6 months and 2½ years of age. The blood is characterized by a normal, high or low red cell count, a low hemoglobin content of the whole blood and marked microcytosis and hypochromia of the erythrocytes. Only a rough relationship is apparent between the lowered hemoglobin value of the whole blood and the alteration of the cells. In samples 1 and 3, with a cell count of 2,980,000 and 5,150,000, respectively, per cubic millimeter, the mean cell volume was identical, 51 cubic microns. If the data relative to samples 4 and 5 are compared, it may be noted that although in sample 5 the cell count and the hemoglobin content of the whole blood were higher than in sample 4, the cells of sample 5 were smaller and contained less hemoglobin. Samples 5 and 6 had 10.1 and 10.6 Gm. of hemoglobin, respectively, per hundred cubic centimeters of whole blood (the borderline of clinically recognized

TABLE 3.—*Data on Blood from Infants with Nutritional Anemia*

	Red Blood Cells			Hemoglobin		
Blood Samples	Count, Millions per Cu. Mm.	Volume of Cells in Whole Blood, Percentage	Mean Cell Volume, Cubic Microns	In Whole Blood, Gm. per 100 Cc.	In Cells, Gm. per 100 Cc.	Mean Hemoglobin Content per Red Cell, Micromicrograms
1	2.98	15.2	51	3.4	22.5	11.5
2	3.98	24.3	61	5.8	23.9	14.6
3	5.15	26.3	51	7.1	27.0	13.8
4	4.60	31.3	68	8.9	28.4	19.3
5	6.23	36.6	59	10.1	27.6	16.2
6	5.11	33.1	65	10.6	32.0	20.7

anemia in infants of the age group under consideration), but there was a considerable difference in the cells of the two samples, as to both size and hemoglobin content.

Figures 1 and 2 illustrate graphically the sequence of changes in these characteristics in samples of blood taken at varying intervals from two seemingly normal infants from birth through the first two years.

Figure 1 represents the study of the blood of a white boy with apparently normal physical development. During two years the red blood cell count ranged between 4,000,000 and 4,500,000 per cubic millimeter. The mean red cell volume decreased from an initial high value, 122 cubic microns, to 80 cubic microns in six months and thereafter remained at approximately that value. The hemoglobin content of the whole blood fell to 10 Gm. per hundred cubic centimeters but rose again to 12 Gm. when the child was about 9 months old and thereafter remained at approximately that value. The hemoglobin concentration in the cells remained fairly constant at about 34 Gm. per hundred cubic centimeters and the changes in the hemoglobin content per cell roughly paralleled those of the size of the cell.

Figure 2 represents the study of the blood of a Negro boy with apparently normal physical development whose blood underwent the typical changes which are observable during the development of and recovery from nutritional anemia in infants. His red cell count fell to 3,600,000 per cubic millimeter when he was 1 month old and thereafter rose and remained at about 5,000,000. The mean red cell volume

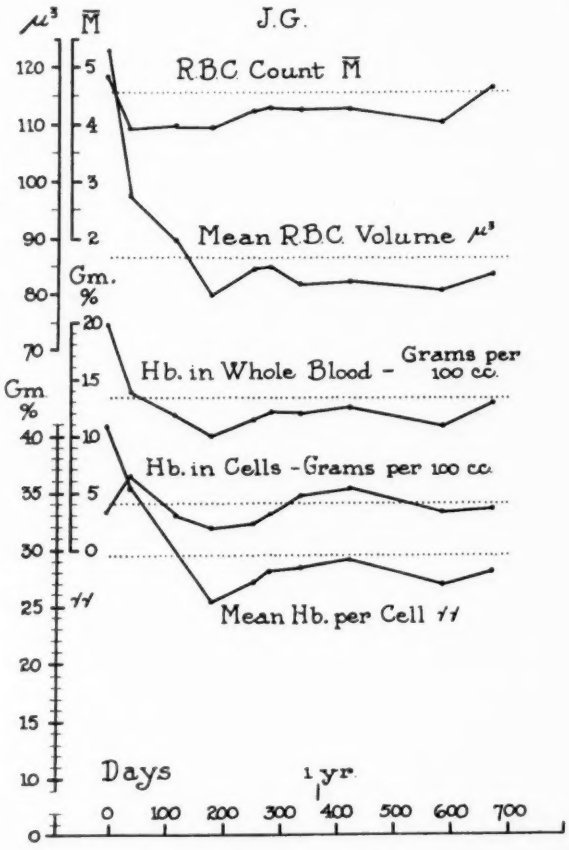

Chart 1.—Curves showing the changes observed in the blood of a white boy apparently normal in general physical development, who was studied from birth to the age of 22 months.

decreased progressively until when he was 8 months old the cells were as small (57 cubic microns) as those found in the blood of patients with more severe, clinically recognized nutritional anemia. The hemoglobin content of the whole blood fell to 6.5 Gm. per hundred cubic centimeters; the hemoglobin concentration in the cells, to 24 Gm., and the mean hemoglobin content per cell, to 14 micromicrograms. When the

boy was 8 months old the administration of iron was started, and a progressive increase in these values followed. Actually the rate of recovery was not as rapid as that which has been observed in many cases in which recognized nutritional anemia was more severe (fig. 3). The slower recovery was apparently due to a series of severe infections of the upper respiratory tract which the child suffered, beginning about forty days after the iron therapy was started.

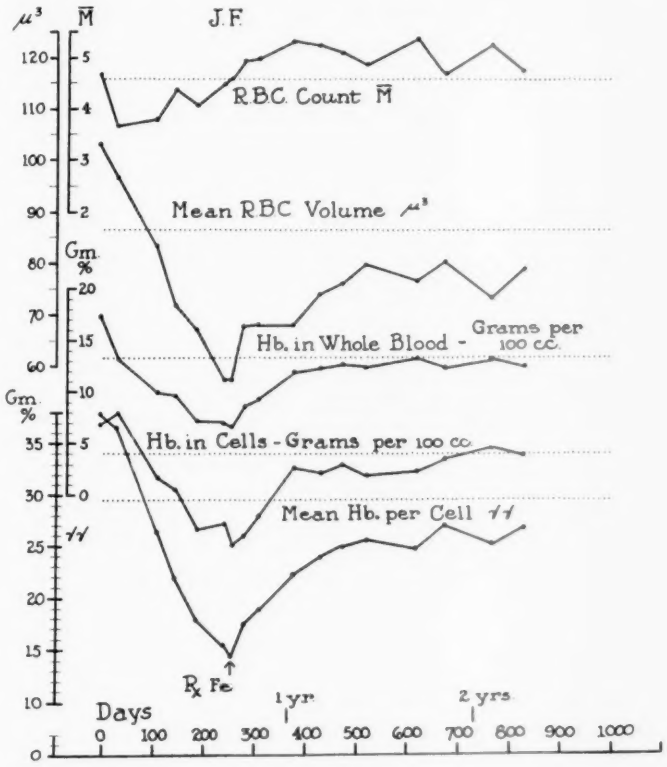

Chart 2.—Curves showing the changes observed in the blood of a Negro boy apparently normal in general physical development, who was studied from birth to the age of 27 months. The development of anemia and the recovery after the administration of iron from the ninth through the twelfth month are illustrated.

In the course of the investigation during which these examples were studied, samples of blood were taken at intervals of approximately three months from a considerable number of infants who were being studied closely from birth through their early years. From the data thus collected an attempt has been made to define the normal and the abnormal limits of variability of the red cell count, the mean red cell volume, the hemoglobin content of the whole blood and the hemoglobin content

in each cell in order better to delineate what constitutes the borderline of clinically significant anemia. Our extensive studies indicate that at one time or another during the age period of from 6 months to 2½ years the red blood cells of a majority of apparently healthy infants show minor alterations which follow the general pattern of the changes illustrated in figure 2. By our method of study, borderline anemia has been demonstrated to occur much more frequently among seemingly normal infants than is generally recognized by most pediatricians. Moreover, evaluated in the terms previously described, anemia when

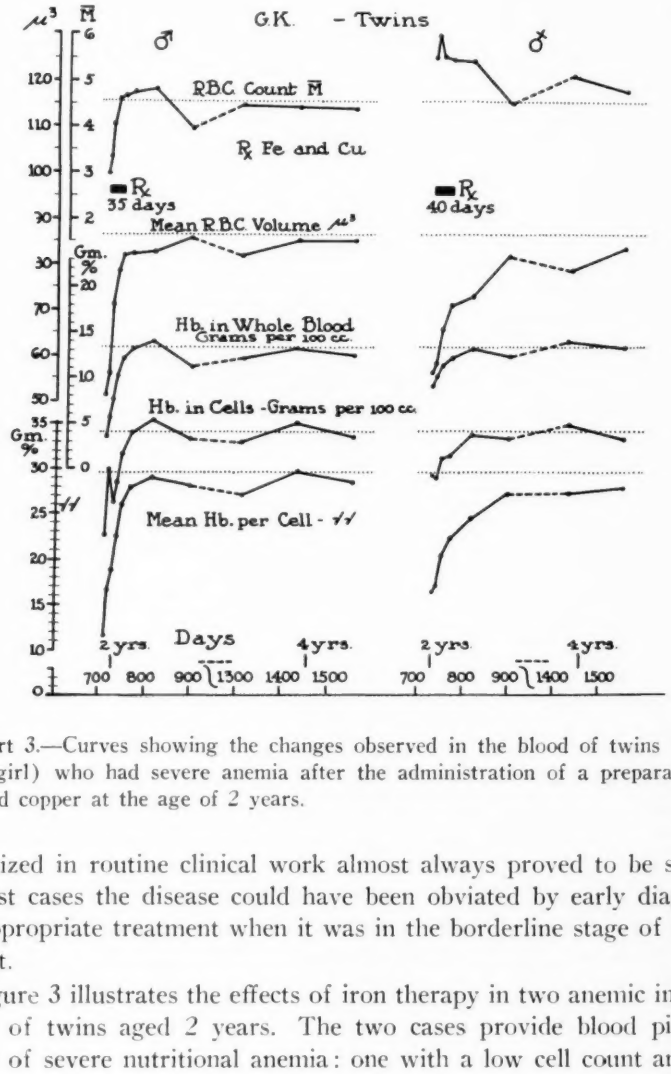
G.K. - Twins
RBC. Count M
℞ Fe and Cu
℞ 35 days
℞ 40 days
Mean R.B.C. Volume
Hb. in Whole Blood Grams per 100 cc.
Hb. in Cells - Grams per 100 cc.
Mean Hb. per Cell - γγ
Days
2 yrs.
4 yrs.
700 800 900 1300 1400 1500
700 800 900 1400 1500

Chart 3.—Curves showing the changes observed in the blood of twins (a boy and a girl) who had severe anemia after the administration of a preparation of iron and copper at the age of 2 years.

recognized in routine clinical work almost always proved to be severe. In most cases the disease could have been obviated by early diagnosis and appropriate treatment when it was in the borderline stage of development.

Figure 3 illustrates the effects of iron therapy in two anemic infants, a pair of twins aged 2 years. The two cases provide blood pictures typical of severe nutritional anemia: one with a low cell count and the

other with a high cell count and both with marked microcytosis and hypochromia. The infants were treated alike, by administration of a preparation of iron and copper for thirty-five and fifty days, respectively, with the results shown in the chart, namely, a rapid change in all values in the direction of normal. The high red cell count of the girl fell to 4,500,000, the value to which the red cell count of her brother rose, and there was a rapid increase in the size and the hemoglobin content of the cells, as well as in the hemoglobin content of the whole blood.

Table 4 contains data summarizing the effects of iron therapy in infants with nutritional anemia. The examples listed were samples of blood from three anemic infants taken before and after a course of iron therapy, the period of treatment being, respectively, five weeks,

TABLE 4.—*Data on Samples of Blood Taken Before and After Iron Therapy from Infants with Nutritional Anemia*

	Red Blood Cells			Hemoglobin		
Cases	Count, Millions per Cu. Mm.	Volume of Cells in Whole Blood, Percentage	Mean Cell Volume, Cubic Microns	In Whole Blood, Gm. per 100 Cc.	In Cells, Gm. per 100 Cc.	Mean Hemoglobin Content per Red Cell, Micromicrograms
1. Before	2.98	15.2	51	3.4	22.5	11.5
After	4.82	39.7	82	13.9	35.1	28.9
2. Before	5.51	30.7	56	8.9	29.1	16.2
After	4.53	36.9	82	12.2	33.1	27.0
3. Before	4.91	33.9	69	10.3	30.4	21.0
After	4.90	41.0	84	14.0	34.1	28.6

six weeks and six months. In the first case the red cell count rose; in the second it fell, and in the third it underwent practically no change. In each case the hemoglobin content of the whole blood increased, and its rise was accompanied by an increase in the mean cell volume, as well as by a rise in the hemoglobin concentration in the cells.

The examples listed in table 4 are cited mainly in order to emphasize one practical point in applying the results of our studies to routine clinical work. When it is not possible or practical to determine the volume of the cells, the value for the mean hemoglobin content per cell, calculated from the hemoglobin content of the whole blood and the cell count, is almost as instructive as the other data. In infants, the changes in the size of the cells and in the hemoglobin content are roughly parallel during the development of and recovery from nutritional anemia. The diminution in the size of the cells occurs earlier than the decrease in the hemoglobin concentration, but the two changes are additive, and both depress the mean hemoglobin content per cell. For clinical purposes it may be assumed that a hemoglobin content of 20

micromicrograms or less per cell justifies a diagnosis of anemia regardless of the hemoglobin content of the whole blood. This value is found frequently in cases of borderline anemia even when the hemoglobin content of the whole blood is above 11 Gm. Adequate treatment with various preparations of iron almost invariably brings about a prompt improvement in such cases as well as in cases in which the disease is more severe.

We cannot attempt to discuss here the much debated questions concerning the choice of therapy, of which many different types are recommended at the present time. It may be suggested, however, that a better evaluation of the preparations of iron and other medicaments now recommended (and debated) may be made after the wider application of a method of study such as we have employed. In the cases cited, in which treatment was given, the patient received either a 12 per cent aqueous solution of iron and ammonium citrates (U. S. P.) or the same solution with 0.8 per cent copper sulfate added. Both solutions were given in doses of about 0.5 cc. per kilogram of body weight. The solution containing copper was given in milk with the meals, because it occasionally provoked vomiting when given otherwise. The solution without copper was given either in milk or in orange juice between meals, and it seems at present that this method for the administration of iron is preferable.

SUMMARY

Accurate determinations of the size and the hemoglobin content of the erythrocytes, in addition to the usual determinations of the cell count and the hemoglobin content of the whole blood, constitute a valuable aid both in the diagnosis and in the control of therapy of nutritional anemia in infants. Nutritional anemia of the iron deficiency type, occurring for the most part in infants between 6 months and 2½ years of age, is characterized by a low hemoglobin content of the whole blood, a variable red cell count (normal, low or high) and microcytosis and hypochromia of the red cells. The microcytosis appears to develop first and to be the most important sign heralding the development of the anemic condition. Iron therapy brings about a rapid increase in the mean size of the cells as well as in the hemoglobin concentration per cell and the hemoglobin content of the whole blood.

Case Reports

CONGENITAL APLASIA OF THE ISLANDS OF LANGERHANS WITH DIABETES MELLITUS

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Diabetes mellitus in infants and children presents problems which do not exist in a study of the disease in adults. Warren [1] stated that the most characteristic pathologic change of the islands of Langerhans in diabetic children is lymphocytic infiltration. In a few cases the number and amount of island tissues are decreased. In a rare case there is apparently absence of cells which may be recognized morphologically as mature islands of Langerhans. The present report presents a case of the latter type.

REPORT OF A CASE

S. T., a 13 year old white girl born in America of Italian parents, was admitted to the New York Hospital because of pain in the side, which had been present for twenty-four hours. (Dr. Eugene DuBois supplied the clinical data.)

Family History.—The father and mother were Italian-born and 44 and 35 years of age, respectively. The mother had had 6 pregnancies, the fourth of which ended in a miscarriage at two months. There were 3 sisters, 18, 16, and 10 years of age, and one brother, 8 years of age, all living and well. There was no history of diabetes in the family.

Past History.—The period of gestation and the birth of the patient were uneventful. The teeth erupted at eight months, and she walked at fourteen months. As a baby she cried a great deal and began begging for water before she could talk. She had measles as a baby, but no other infectious disease was reported by the parents. Menstruation had not started. She went to school at six years but was forced to leave after the second year because of failing vision and inability to read and write.

Present Illness.—Polydipsia was noticed by the mother before the second birthday. When the patient was 4 years old she had spastic paralysis of the legs for two weeks. When she was 7 the family physician made a diagnosis of diabetes because of increasing polydipsia and polyuria. A short time later this diagnosis was confirmed at the New York Post-Graduate Medical School and Hospital. For the past six years no systematic treatment had been given and the symptoms had continued, together with progressive loss of weight. For the

From the Department of Pathology of the New York Hospital, New York, and the Cornell University Medical College, Ithaca, N. Y.

1. Warren, S.: The Pathology of Diabetes Mellitus, Philadelphia, Lea & Febiger, 1930.

past six months the appetite had been poor. Three days before admission the patient complained of pain in the "stomach," which during the last day was localized in the lumbar region.

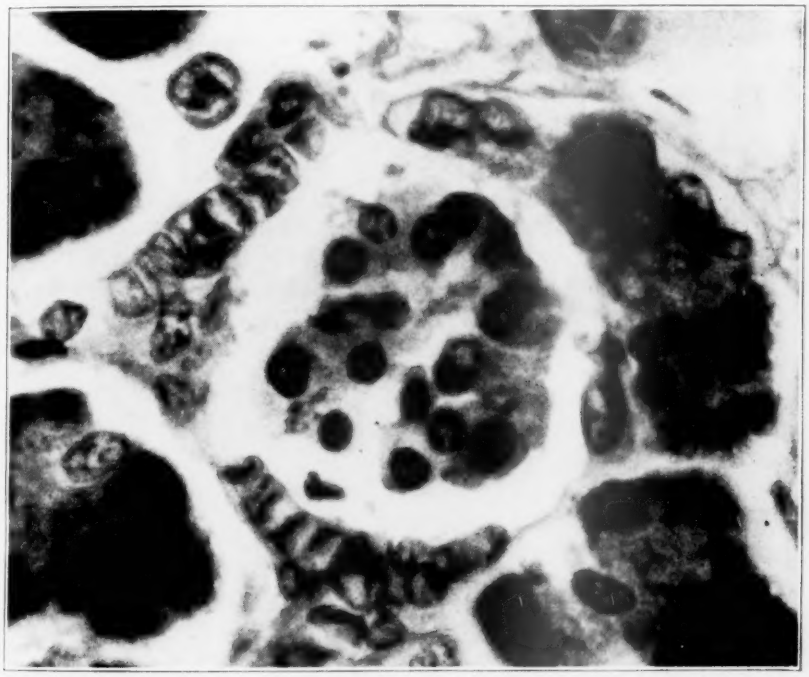
Physical Examination.—The patient was emaciated, undernourished and underdeveloped. The hair of the axillae and pubis was not developed. The pupils were normal, but there was gross impairment of vision and the fundi could not be visualized. The teeth were carious. There was a blowing systolic murmur over the entire precordium, heard best at the apex. The blood pressure was 108 systolic and 84 diastolic. There were slight tortuosity and marked thickening of the peripheral arteries. The bladder extended 8 cm. above the symphysis. The deep reflexes were hypo-active. The external genitalia were infantile. Ophthalmoscopic examination by Dr. Bernard Samuels revealed bilateral diabetic cataracts.

Laboratory Examinations.—The urine varied from 1.001 to 1.008 in specific gravity. Albumin and large numbers of white cells were almost constantly present. Glycosuria was usually present. The white blood cell count varied from 6,600 to 24,400, the red cell count from 3,600,000 to 4,000,000 and the hemoglobin content from 66 to 76 per cent (9.8 to 11.0 Gm. per hundred cubic centimeters). The percentage of mature polymorphonuclear cells of the blood varied from 32 to 73 and of the immature cells from 18 to 34. The number of eosinophilic leukocytes rose to 10 per cent at one time but was usually from 1 to 2 per cent. In 8 determinations of blood pressure the systolic varied from 130 to 119 and the diastolic from 111 to 79. The urea nitrogen content varied from 9 to 30 mg. per hundred cubic centimeters. When the patient was admitted the cholesterol content was 151 mg. per hundred cubic centimeters, and after two months it rose to 327 and 341 mg. The calcium content was 8.8 mg. and 9.8 mg., and the phosphorus content 4.8 mg. and 5.1 mg., per hundred cubic centimeters. The Kline test gave negative results. Electrocardiographic examination revealed an increased amplitude of P_2 and P_3 and a low amplitude and spitting of R_1. A culture of the urine showed Streptococcus haemolyticus. There were less than 4 rat units of ovarian follicular hormone per liter of urine. Roentgen examination revealed a slight degree of decalcification of the long bones, increase of the hilar shadows and a normal base of the skull and sella turcica.

Course.—The manifest infection of the urinary tract was treated with an indwelling catheter and irrigations with boric acid twice daily. The diabetes was treated with a diet of 100 Gm. of protein, 75 Gm. of fat and 300 Gm. of carbohydrate, divided into 4 meals, with a total caloric intake of 2,300. This was supported by insulin four times daily in doses of 15, 10, 10 and 15 units. At intervals sugar appeared in the urine, and the dosage of insulin was increased in four stages to 30, 10 and 20 units. After some days with this dosage the patient excreted from 55 to 77 Gm. of sugar daily in the urine, and the blood sugar content varied from 180 to 290 mg. per hundred cubic centimeters. Acetone never appeared in the urine, and symptoms of acidosis were not observed. The daily urinary volume ranged from 9,000 to 10,000 cc. Pitressin in doses of 0.2 cc. given three times a day for three days reduced the volume to from 3,000 to 5,000 cc. There was a gradual increase in weight from 15.6 to 19 Kg. in three months. Three months after admission, during an uneventful period, twitching of the left leg, which rapidly spread to the right leg, appeared simultaneously with loss of consciousness. The urine contained sugar but not acetone. Intravenous injections of dextrose and insulin and 5 per cent calcium gluconate were of no avail, and death occurred one hour later.

Autopsy.—Examination was performed ten hours after death by Dr. Peter Midelfart.

Gross Examination: The serous cavities were normal. The heart weighed 125 Gm. and aside from atheromatous plaques on the mitral valve was without pathologic change. The aorta and its branches showed a few atheromatous plaques. The thymus was small and firm. The thyroid gland was of the usual size and on section showed little colloid. There were small calcified nodules in the subpleural tissue of the upper lobe of the right lung, but the lungs were otherwise normal. The spleen weighed 105 Gm. and showed a localized thickening of the capsule. The splenic substance appeared normal. The gastro-intestinal tract, liver and biliary ducts revealed no deviation from normal. The adrenals each weighed 4.5 Gm. The cortex and medulla were distinct and of the usual structure. The pancreas was of the usual size and shape. A section revealed the usual lobular



Photomicrograph of a section of the pancreas, showing a small group of cells which have the morphologic characteristics of island cells. No larger masses than this were found in the entire pancreas (× 1200).

architecture without gross pathologic change. The kidneys each weighed 190 Gm. The pelves were dilated and filled with a purulent exudate. The kidney substance was decreased in thickness and had small hemorrhagic areas throughout it. The ureters were dilated and tortuous, measuring 3 cm. in circumference. The surface of the bladder was swollen and red, and the wall was thickened. The uterus was small, measuring 12 by 5 by 5 mm. The ovaries measured 5 mm. at their greatest diameter. The brain showed no gross pathologic change. The pituitary gland was of the usual size but was flattened slightly in the anteroposterior direction.

Microscopic Examination: The liver, spleen, heart and lungs showed no significant deviation from normal structure. The thyroid acini were small and

contained little colloid. The interstitial tissue was abundant. The adrenal glands showed no microscopic change. The ovaries showed a few primordial follicles embedded in typical ovarian stroma. The media of the aorta revealed slight chromotropic degeneration without cyst formation. The kidneys, ureters and bladder showed the usual histologic changes of a chronic inflammatory process. The glomeruli and tubules of the renal cortex showed no evidence of primary renal disease.

Sections from the tail, body and head of the pancreas were distinctly lobulated. The interlobular connective tissue was loose and the lobulation was that of immaturity rather than that of secondary fibrosis. Within the lobules the interstitial tissue was abundant and infiltrated with a few lymphocytes. The acinar tissue was without pathologic change. The intercalated ducts were inconspicuous. The larger ducts showed the usual structure. Islands of Langerhans of normal structure and size were not present. A thorough study of numerous sections revealed a few small cell groups morphologically similar to insular cells (fig.). The cells of these groups varied from 10 to 18 mm. in diameter, were polygonal or round and were not arranged in any definite pattern. The cytoplasm was homogeneous and acidophilic. The nuclei were relatively small and highly chromatic. Fixation was not carried out, so the specific cell granules could be studied.

A count of 16,755 cells in the pituitary gland at all levels by Dr. Robert J. Parsons showed 58.2 per cent chromophobe cells, 27.8 per cent acidophils and 14 per cent basophils. Sections which included the infundibulum, the optic chiasm, the lamina terminalis, the anterior commissure, the massa intermedia, the posterior commissure, the pineal body, the lamina quadrigemina, the nuclei and fiber tracts beneath the aqueduct of Sylvius and the posterior portion of the third ventricle, and the mamillary bodies showed no pathologic change.

Bacteriologic Examination: A culture of blood removed from the heart at autopsy was sterile.

COMMENT

The exact term which should be applied to the pathologic change in the pancreas may be questioned. Aplasia, failure of development of an intact anlage, and hypoplasia, failure to grow to the expected size but with adequate physiologic development of each unit, are possible terms. Agenesia, or failure of the formation of an anlage, is not applicable since a few islet cells are present. It is possible that some disease before the second year of life resulted in destruction of the islands, but the absence of any residuum of this process and the manifest general immaturity of the organ do not support this conception. The history of the case is consistent with a congenital defect, and in view of the severe physiologic disturbance the explanation of congenital aplasia as the etiologic factor appears most probable. There was no gross or microscopic evidence as to the nature and pathogenesis of this anomaly. The acinar tissue was seemingly capable of normal physiologic function, since fat was digested.

An apparent decrease of the number of islands of Langerhans in diabetes is not an uncommon finding. Opie,[2] reporting on 19 cases of

2. Opie, E. L.: Disease of the Pancreas, Philadelphia, J. B. Lippincott Company, 1903.

diabetes, recorded the islands as "scant in number" in 2. One of these 2 cases, that of a girl 14 years of age, was reported separately by Pleasants [3] and occurred in a family in which there were 6 instances of diabetes. Of the 90 cases studied by Cecil,[4] in 20 there was a decrease in the number of islands. In 15 of these there was an associated chronic interacinar pancreatitis not present in the other 5. Cecil stated the belief that the decrease in the one type was a destruction incident to the pancreatitis and in the other was to be regarded as a congenital anomaly. In his study of the pancreas in 259 cases, Warren [1] reported an apparent decrease in the number of islands in 51. In none, however, were they absent. In all of the 18 cases reported by Weichselbaum and Stangl,[5] atrophy of the pancreas was present, with a decrease of islands. The authors emphasized the fact that this decrease in pancreatic atrophy with diabetes is in striking contrast to the retention of normal islands in all other types of atrophy. Kasahara [6] studied the pancreas microscopically in 83 routine autopsies. Among 3 cases of diabetes there was a decrease in the number of islands in 1, but a similar decrease was present in 2 cases in which the patient had not had diabetes. In a report of 13 instances of diabetes, Szobolew [7] stated: "In 4 Fällen konnte ich die Inseln überhaupt nicht finden, in den übrigen 9 Fällen dagegen wurde eine bedeutende Verringerung ihrer Zahl bis zu fast gänzlichem Fehlen beobachtet." ("In 4 cases it was impossible for us to find the islands at all, and in the other 9 cases their number was so reduced that they appeared almost to be absent.") Dieckhoff [8] also reported absence of islands in a case in which the patient had been addicted to the use of alcohol and had had diabetes for eleven years. The value of this finding may be questioned since Dieckhoff also failed to find islands in 2 cases in which diabetes was not present.

From this review it is apparent that a decrease in the number of islands in diabetes is a well established finding and occurs in about 20 per cent of all cases. It is significant that absence of the islands

3. Pleasants, J. H.: Heredity in Diabetes Mellitus, with a Report of Six Cases Occurring in a Family, Bull. Johns Hopkins Hosp. **11**:325, 1900.

4. Cecil, R. L.: A Study of the Pathological Anatomy of the Pancreas in Ninety Cases of Diabetes Mellitus, J. Exper. Med. **11**:266, 1909.

5. Weichselbaum and Stangl, E.: Zur Kenntnis der feineren Veränderung des Pankreas bei Diabetes mellitus, Wien. klin. Wchnschr. **14**:968, 1901.

6. Kasahara, M.: Ueber das Bindegewebe des Pankreas bei verschiedenen Krankheiten, Virchows Arch. f. path. Anat. **143**:111, 1896.

7. Szobolew, L. W.: Zur normalen und pathologischen Morphologie der inneren Secretion der Bauchspeicheldrüse, Virchows Arch. f. path. Anat. **168**:91, 1902.

8. Dieckhoff, C.: Beitr. z. wissensch. Med., Festschr. Theo. Thierfelder, 1895, p. 95; quoted by Szobolew.[7]

has not been reported since the early studies of Szobolew in 1902 and Dieckhoff in 1895.

In contrast, congenital hypoplasia of the pancreas as a whole is rare. Kriss [9] collected reports of 4 instances from the literature and added 2 of his own. In 3 of the 6 cases the lesion was associated with diabetes. In all instances the hypoplasia was apparently the result of complete absence of the dorsal pancreatic anlage which forms the body and tail of the adult pancreas.

SUMMARY

A case of congenital diabetes associated with aplasia of the islands of Langerhans in a girl 13 years of age is reported.

9. Kriss, B.: Zur Kenntnis der Hypoplasie des Pankreas, Virchows Arch. f. path. Anat. **263**:591, 1927.

MACROCYTIC HYPERCHROMIC ANEMIA IN EARLY INFANCY

REPORT OF A CASE AND REVIEW OF THE LITERATURE

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During the past two decades exhaustive investigation has helped clarify many phases of the problem of infantile anemia. Deficiency and hemolytic anemia have been rather definitely differentiated, and each type in turn has been subdivided in an attempt to analyze further and to understand the pathogenesis involved. Investigations of microcytic hypochromic anemia have been comparatively thorough, probably because of its great frequency. On the other hand, the macrocytic hyperchromic type of deficiency anemia has been less completely studied, owing to its comparative rarity. In this paper a case of macrocytic hyperchromic anemia in an infant aged 9 months is reported, and the literature on similar anemia in patients under 1 year of age is reviewed.

REVIEW OF THE LITERATURE

Reports of cases of macrocytic hyperchromic anemia in early infancy have been scanty. Indeed, Blackfan,[1] Cooley and Lee,[2] Naegeli[3] and others stated the belief that pernicious (Addison-Biermer's) anemia had never been described in a patient under 1 year. Von Starck[4] in 1909 reported the first case, in a 6 month old infant with macrocytic anemia. A year later Koch[5] described a case in a patient aged 8 months, who died after five weeks. The author stated that while the condition was suggestive of pernicious anemia, there

From the Pediatric Service of Dr. C. S. Boyd, the New York City Hospital, Welfare Island.

1. Blackfan, K. D., in discussion on Cooley and Lee.[2]

2. Cooley, T. B., and Lee, P.: "Pernicious" Blood Pictures in Infancy, J. Pediat. **1**:184 (Aug.) 1932.

3. Naegeli, O.: Blutkrankheiten und Blutdiagnostik: Lehrbuch der klinischen Hämatologie, ed. 5, Berlin, Julius Springer, 1931.

4. Von Starck, W.: Die basophile Granulation (Punktierung) der roten Blutkörperchen im embryonalen Blut und bei anämischen Zuständen im Kindesalter, Jahrb. f. Kinderh. **69**:264, 1909.

5. Koch, G.: Ueber perniziöse Anämie und extramedulläre Blutbildung im Säuglingsalter, Jahrb. f. Kinderh. **71**:140, 1910.

were other causes for a similar blood picture: infection, congenital syphilis, rickets and chronic malnutrition with inadequate storage. Faber [6] in 1928 described two cases of macrocytic anemia in patients under 1 year. He concluded that whether or not true pernicious anemia occurred before the age of 1 year, anemia in which erythroblastic maturation was defective or inadequate might occur as early as the sixth week and responded strikingly to liver therapy. Gerbasi [7] reported a case of such anemia in an 11 month old infant in 1929. Two more cases were added by Ducas and Jacquet [8] in 1931. Páez de la Torre [9] in 1932 reported two additional cases, in one of which the patient responded well to liver therapy. In the same year Cooley [2] described eight cases in which the infant responded to transfusions. A summary of the preceding cases may be found in table 1.

The occurrence of macrocytic anemia associated with other diseases of infancy is extremely infrequent. Nutritional [10] and alimentary [11] anemia are mainly microcytic and hypochromic. Parsons,[12] however, has expressed the belief that the more severe forms of goat's milk anemia are characterized by the presence of megaloblasts in the blood stream and represent a deficiency anemia probably allied to the megalocytic form of anemia seen in some cases of Gee's disease.[13] Macrocytic

6. Faber, H. K.: Value of Liver Extract (343) in Identifying and in Treating Certain Anemias of Infancy and Childhood, Am. J. Dis. Child. **36**:1121 (Dec.) 1928.

7. Gerbasi, M.: Anemia perniciosa rigenerativa tipo Biermer in un lattante, Pediatria **37**:1343 (Dec. 15) 1929.

8. Ducas, P., and Jacquet, J. M.: Deux cas d'anémies graves précoces chez le nourrisson, Arch. de méd. d. enf. **34**:420 (July) 1931.

9. Páez de la Torre, J. M.: Anemia de Biermer observada en tres niños en el curso del año 1932, Semana méd. **2**:1822 (Dec. 15) 1932.

10. Steen, R. E.: Nutritional Anaemia of Infancy: Comparison with Chronic Microcytic Anaemia of Women During Child-Bearing Period, Irish J. M. Sc., September 1934, p. 527.

11. Hymanson, A.: Alimentary Anemia, Arch. Pediat. **47**:267 (May) 1930. Lorio, C.: Alimentary Anemia in Infants and Its Treatment, New Orleans M. & S. J. **82**:432 (Jan.) 1930.

12. Parsons, L. G.: Studies in Anaemias of Infancy and Early Childhood; Introduction, Arch. Dis. Childhood **8**:85 (April) 1933.

13. (*a*) Parsons, L. G., and Hawksley, J. C.: Studies in Anaemias of Infancy and Early Childhood: Anhaematopoietic Anaemias (Deficiency Diseases of the Erythron); Nutritional Anaemia, and Anaemias of Prematurity, Scurvy and Coeliac Disease, Arch. Dis. Childhood **8**:117 (April) 1933. (*b*) Vaughan, J. M., and Hunter, D.: Treatment by Marmite of Megalocytic Hyperchromic Anaemia Occurring in Idiopathic Steatorrhoea (Coeliac Disease), Lancet **1**:829 (April 16) 1932. (*c*) Bennett, T. I.; Hunter, D., and Vaughan, J. M.: Idiopathic Steatorrhea (Gee's Disease): A Nutritional Disturbance Associated with Tetany, Osteomalacia and Anemia, Quart. J. Med. **1**:603 (Oct.) 1932.

TABLE 1.—*Recorded Cases of Macrocytic Hyperchromic Anemia of Infancy*

Average

TABLE 1.—*Recorded Cases of Macrocytic Hyperchromic Anemia of Infancy*

Author	Year	Case No.	Age, Mo.	Average Percentage Hemoglobin	Average R.B.C., Millions	Color Index	Gastric HCl	Elevated Icterus Index	Spleen	Liver	Immature R.B.C.	Therapy	Reticulocyte Response	Improvement: Spleen	Improvement: Liver	Improvement: Blood	Recurrence Without Further Therapy
Von Starck	1909	..	6	25	1.2	1.04	?	?	Palp.	Palp.	Many	Mother's milk	?	Death in 1 month			....
Koch*	1910	..	8	25	1.1	1.18	?	No	Not palp.	Not palp.	Many	Cow's milk	?	Death in 5 weeks			....
Faber	1928	1†	9	16	0.65	1.23	Low then absent	No	Palp.	Palp.	Many	Liver extract	Good	No	?	Cure	Hypochromic 2d degree anemia in 1 mo.
		2‡	3	51	2.4	1.06	Low	Yes	Palp.	Palp.	Few	Liver extract	Fair	?	?	Only R.B.C. increased	None in 3 mo.
Gerbase	1929	1	11	32	1.5	1.33	?	?	Palp.	Not palp.	None	Liver extract	?	Cure	...	R.B.C. increased more than hemoglobin	?
Ducas and Jacquet	1931	1§	1	30	0.54	3.0	?	?	Palp.	Not palp.	Many	Sulfarsphenamine, liver extract, transfusions	?	Cure	...	Cure	No recent recurrence
		2§	8	35	2.36	0.7	?	?	Not palp.	Not palp.	None	Sulfarsphenamine, liver extract	?	.....	...	R.B.C. not imp., hg. to 50%, color ind. to 1	....
Cooley and Lee	1932	1	3	24	1.6	0.75	?	?	Palp.	?	Few	Transfusions	?	?	?	Cure	?
		2	4	24	1.5	0.80	?	?	Not palp.	Not palp.	Few	Transfusions	?	No	No	Improv.	?
		3	5	24	0.9	1.33	?	?	Not palp.	Not palp.	Few	Transfusions	?	No	No	Cure	?
		4‖	5	23	1.2	0.96	?	?	Palp.	Not palp.	Mod.	Transfusions	?	Death in 4 days			....
		5	7	12	1.0	0.60	?	Yes	Palp.	Palp.	Many	Transfusions	?	Cure	Cure	Cure	None in 5 years
		6¶	10	30	1.6	0.94	?	?	Palp.	Not palp.	Mod.	Transfusions	?	?	...	Improv.	No
		7#	10	20.9	1.2	1.20	?	?	Palp.	Palp.	Few	Transfusions	?	?	?	Cure	?
		8**	11	27	2.5	0.54	?	No	Not palp.	Not palp.	Many	None	..	Death in 1 day			....
De La Torre	1932	1††	1½	28	1.0	1.4	?	?	?	?	?	Symptomatic	?	Death in 4 months			....
		2††	4	50	2.2	1.13	?	?	Palp.	Not palp.	?	Liver extract	?	?	...	Cure	?
Author's case.....		9	75	3.3	1.12	Low	No	Palp.	Palp.	Mod.	Iron Liver extract	No Good	Slight Cure	Slight Cure	Slight Cure	None in 1 year	

* Autopsy observations: The spleen was moderately enlarged, showing lymphoid hyperplasia; the femoral pulp and the liver showed enormous numbers of megaloblasts, normoblasts and very young leukocytes; very few normal red blood cells were present; blasts had 1, 2 or 3 nuclei.

† There was a history of vomiting, diarrhea and partial goat's milk diet; hypochromic secondary anemia was present on the second admission; a marked rise in weight appeared after the use of liver therapy; the value of iron in primary anemia was illustrated.

‡ The hemoglobin content was lower after liver therapy than on admission; the value of iron in primary anemia was again demonstrated.

§ Hemoglobin content was measured by Tallqvist hemoglobinometer only.

‖ Autopsy observations: The bone marrow showed marked megaloblastic and macrocytic activity; the spleen showed areas of myeloid metaplasia.

¶ Six weeks of severe furunculosis preceded anemia.

\# Intercurrent infection was present while the patient was in the hospital.

** There was a history of examthem followed by a cough; a head injury was sustained one month prior to admission; signs of intracranial hemorrhage were present; the blood picture was like that of erythroblastic anemia, showing achromia, poikilocytosis, many normoblasts, a moderate number of macroblasts and no true megaloblasts; the bone marrow was atrophic; the spleen showed myeloid metaplasia.

†† There was a history of severe prolonged gastro-intestinal disturbances.

hyperchromic anemia occurs rarely in patients with celiac disease and has never been reported in a patient under 1½ years of age. Parasitic infestations may cause macrocytic anemia in infants; the picture is identical with that seen in adults.[14]

REPORT OF CASE

D. U., a Jewish boy born on Dec. 29, 1933, at the New York City Hospital, was admitted nine months later, on Oct. 3, 1934, to the pediatric service of Dr. C. S. Boyd because of failure to gain weight, pallor and a mass in the abdomen.

History.—The family history revealed no pertinent data. The mother and the father had always been well. No history of tuberculosis, syphilis, blood dyscrasias or other familial disease was elicited. The patient was the mother's first child, and the antepartum course had been uneventful. Delivery was at full term by version and breech extraction for transverse position, after a seventy-two hour labor. No immediate injuries were evident, and the child appeared normal. The weight at birth was 8¼ pounds (3,742.12 Gm.).

The infant was breast fed for two weeks and then placed on a formula of whole milk and cane sugar, with the gradual addition of small amounts of cereal and cod liver oil. At 4½ months, because of financial difficulties at home, the child was sent to a charity nursery. His weight was then 13½ pounds (6,123.48 Gm.). Almost immediately a severe attack of vomiting and diarrhea developed, necessitating the patient's transfer to a hospital. Records of that institution show him to have had acute intestinal intoxication and bilateral acute suppurative otitis media. He was treated with a starvation diet, transfusion and parenteral administration of fluids. Bilateral myringotomy was performed. Both the conditions responded well. Vomiting and diarrhea ceased; the formula was gradually increased, and the baby was discharged after four weeks. A blood count at that time revealed 109 per cent hemoglobin and 4,700,000 erythrocytes. The liver and the spleen were not palpable.

Soon after leaving the institution the infant suffered a recurrence of severe diarrhea—ten watery stools daily—and began again to vomit frequently. His weight diminished to 11 pounds (4,989.51 Gm.). At 6 months of age (July 1934) concentrated feedings were begun with condensed milk and evaporated milk. The symptoms gradually lessened. Small amounts of cod liver oil and tomato juice were added during the following month. The infant's weight at 7 months was 10 pounds (4,535.92 Gm.). During the two months prior to his admission to the New York City Hospital other foods were slowly added to his diet, so that at the time of admission it contained evaporated milk, cereal, viosterol, bananas and small amounts of tomato juice. Although his bowels were regular during that period, his appetite was poor and he vomited frequently.

Three weeks prior to the child's admission the mother first noticed a mass in the left side of his abdomen. At his admission she stated that he had always been pale but that pallor had become severe during the four preceding months. The patient had never been observed to have icterus, purpuric lesions, bleeding or unexplained bouts of fever.

Physical Examination.—On admission the patient appeared emaciated and chronically ill and weighed 12½ pounds (5,669.89 Gm.). The skin was markedly pale,

14. Birkeland, I. W.: "Bothriocephalus Anemia," Diphyllobothrium Latum and Pernicious Anemia, Medicine **11**:1 (Feb.) 1932.

cold, moist and of poor turgor. No purpura, ecchymosis, lesion or icteric tint was present. There was generalized moderate lymphadenopathy. The anterior fontanel measured 4 by 2 cm. The pupils were equal and regular and reacted well to light. The conjunctivae were not pale, and the fundi appeared normal. The tonsils were of normal size and appearance. Two upper incisors were present, carious and notched. Skeletal examination revealed that the extremities were disproportionately long. Beading of the ribs was absent. Neurologic examination gave negative results. The heart was normal and the lungs clear throughout. The abdomen was protuberant and slightly distended. No dulness in the flanks or fluid wave was present. The margin of the liver was 2.2 cm. below the right costal arch. The spleen was hard, nontender and freely movable and was felt 4.5 cm. below the left costal margin. The temperature and pulse were normal. A blood count revealed 3,480,000 erythrocytes and 10,900 leukocytes per cubic millimeter, a hemoglobin content of 83 per cent (Sahli) and a color index of 1.11. Smears showed marked macrocytosis, hyperchromia, anisocytosis and polychromasia and moderate poikilocytosis. Five blasts per hundred white blood cells were present.

Progress.—Three days after admission, on October 6, the patient's weight was 11¾ pounds (5,329.7 Gm.). He was put on a formula of 15 ounces (444 cc.) of evaporated milk, 1½ ounces (42.52 Gm.) of dextrimaltose no. 1 and 15 ounces (444 cc.) of water, with small amounts of cereal and orange juice added. The energy quotient was 66 plus. Beginning on October 9, 1 drachm (3.7 cc.) of a 25 per cent solution of iron and ammonium citrates was administered twice daily. On October 10 the daily administration of 2 drachms (7.4 cc.) of cod liver oil and ultraviolet irradiation in gradually increasing doses were begun. By October 15 the liver was barely palpable and the edge of the spleen was only 2.2 cm. below the costal margin. The infant had an excellent appetite and took feedings hungrily, but he gained no weight, and his spleen remained in the same position. The anemia remained the same as on admission, although nucleated red blood cells were no longer present. Gastric analysis revealed hypochlorhydria and the presence of pus clumps in the secretion. On October 26 the red blood cells numbered 3,270,000, and the hemoglobin content was 81 per cent. Macrocytosis was still marked. The weight on October 30 was 12¼ pounds (5,556.49 Gm.).

Daily oral administration of the extract of 50 Gm. of whole liver [15] was begun on October 30. Six days later the reticulocyte count had risen from 3.4 per cent to 8.4 per cent and the red blood cell count to 4,720,000, and in fifteen days the hemoglobin content had increased to 84 per cent. The red blood cells were definitely smaller. The blood remained normal during the rest of the patient's stay at the hospital. The weight, which had not changed during the first month, rose phenomenally after the administration of liver extract. The child gained 7 pounds (3,175.14 Gm.) in a little over three months despite the fact that his total caloric intake did not change and his energy quotient therefore fell rapidly from 66 plus on October 30 to 44 on discharge. He left the hospital on Jan. 29, 1935, at 13 months, weighing 18 pounds and 10 ounces (8,448.14 Gm.). The spleen was now barely palpable. On discharge the red blood cells numbered 4,910,000, and the hemoglobin content was 92 per cent. A smear of blood appeared normal.

After the patient's discharge, the administration of liver extract and of iron was discontinued, and the child was sent to the country, where he received large amounts of sunlight and fresh air. His diet consisted of evaporated milk, cereals,

15. The liver extract was obtained from Eli Lilly & Company.

vegetables, broths, eggs and fruit juices, but it was entirely devoid of meats or meat extractives. He remained entirely well, became active and bright and rapidly learned to walk and talk. At 16 months he had measles, recovering uneventfully. One month later (May 30, 1935) he was brought to the hospital with impetigo. Examination at that time revealed a well nourished infant weighing 25⅔ pounds (11,642.19 Gm.). Mild facial impetigo was present. The lymph nodes were not palpable. The liver and the spleen could not be felt. The remainder of the examination had negative results. Examination of the blood showed: erythrocytes, 5,110,000; hemoglobin, 86 per cent, and leukocytes, 8,840. The red blood cells were normal. Gastric analysis revealed a normal amount of hydrochloric acid and the absence of inflammation. One week after admission the patient was discharged, cured of his dermatitis.

The child returned again at 20½ months for a routine health examination. His development and health were excellent. Meat and meat extractives had been added to his diet. Examination revealed no abnormal findings. Pallor was not

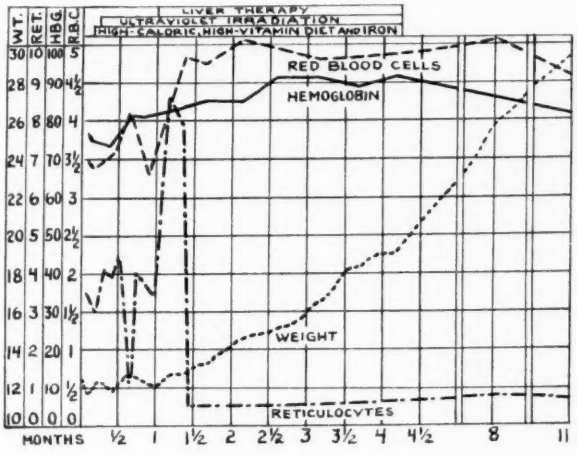

Chart showing the blood and weight curves of the patient during therapy. The abbreviations used are as follows: *WT.*, weight in pounds; *HBG.*, percentage of hemoglobin; *RET.*, percentage of reticulocytes; *R.B.C.*, millions of red blood corpuscles per cubic millimeter.

present. The liver and the spleen were not palpable. A blood count showed 4,670,000 erythrocytes per cubic millimeter and 81 per cent hemoglobin. A smear of blood was normal.

Laboratory Data.[15a]—First Admission: Repeated examinations of the urine gave normal results. Bile and excessive urobilinogen were absent. Reactions to the Wassermann, Schick, Dick and Mantoux tests were negative. Repeated analyses of the blood showed normal amounts of nonprotein nitrogen, urea nitrogen, sugar, chlorides, cholesterol and cholesterol esters. The icterus index was 3. The van den Bergh test gave negative direct and normal indirect reactions. The phosphorus content of the blood was 4.4 mg. and the calcium content 9.5 mg. per

15a. The weight curve and the complete blood picture may be found in chart 1 and table 2.

TABLE 2.—*Blood Picture While the Patient Was Under Observation*

	Date	R.B.C., Millions	Hemoglobin, Percentage (Sahli)	Color Index	Volume Index	Reticulocytes, Percentage	Immature R.B.C. per 100 W.B.C.		W.B.C., Thousands	Granular Leukocytes, Percentage			Lymphocytes, Percentage	Monocytes, Percentage	Other W.B.C., Percentage
							Macroblasts	Normoblasts		Mature	Late Immature	Early Immature			
Liver Therapy; Ultraviolet Irradiation; High Calorie, High Vitamin Diet and Iron Therapy	10/ 5/34	3.48	83	1.11	1.16	3.4	3	2	10.9	18	6	0	72	0	4
	10/ 8/34	3.34	75	1.12	....	3.0	2	1	13.7	17	19	5	56	3	2
	10/10/34	....	..	....	....	4.2	..	..	..	....	..	..	..	..	..
	10/15/34	3.64	74	0.97	0.94	3.7	0	0	12.4	7	4	0	82	5	2
	10/17/34	....	..	....	....	4.6	..	..	..	....	..	..	..	..	..
	10/19/34	....	..	....	....	1.65	..	..	..	....	..	..	..	..	..
	10/22/34	4.13	81	0.98	....	4.1	0	0	12.8	6	7	0	81	4	2
	10/26/34	3.27	81	1.26	....	3.8	0	0	17.7	16	24	0	49	9	2
	10/30/34	....	..	....	....	3.4	..	..	..	....	..	..	..	..	..
	11/ 4/34	....	..	....	....	8.4	..	..	..	....	..	..	..	..	..
	11/ 6/34	....	..	....	....	7.2	..	..	..	....	..	..	..	..	..
	11/13/34	4.72	84	0.89	....	0.5	0	0	15.85	17	4	1	50	26	2
	11/19/34	4.83	85	0.88	....	...	..	..	..	....	..	..	..	..	..
	12/ 2/34	5.01	83	0.82	....	0.7	..	..	..	....	..	..	..	..	..
	12/ 6/34	4.92	92	0.93	....	...	..	..	..	....	..	..	..	..	..
	12/29/34	4.83	91	0.94	....	...	..	..	..	....	..	..	..	..	..
	1/14/35	4.86	89	0.91	....	...	..	..	..	....	..	..	..	..	..
	1/29/35	4.91	92	0.94	....	...	..	..	..	24	13	0	54	5	4
	6/ 4/35	5.11	86	0.84	....	0.8	0	0	8.84	32	3	0	59	3	3
	9/11/35	4.67	81	0.87	....	0.7	0	0	16.15	22	5	0	57	9	7

hundred cubic centimeters. Two weeks after a high vitamin, high caloric diet was instituted, the phosphorus content was 5.5 mg. and the calcium content 10 mg. per hundred cubic centimeters. The bleeding and the coagulation time were normal. The platelets numbered 270,000 per cubic millimeter. The fragility test showed hemolysis to begin with a 0.38 per cent solution of sodium chloride and to be complete with a 0.26 per cent solution. Examination of the stools showed no blood, pus or parasites. The gastric analysis gave the results shown in table 3. (Inflammation in the upper respiratory tract was not present.) One-tenth milligram of histamine hydrochloride was injected during the tests.

Microscopic examination showed large amounts of mucus, many pus cells, some of them in clumps, occasional red blood cells and moderate numbers of round epithelial and yeast cells.

Roentgenographic examination (Dr. George Plehn) showed increased trabeculation of the long bones of the extremities, indicating decalcification. This was particularly marked in the small bones of the hands, where the medulla showed almost cystic formation. Similar blood pictures may be seen in erythroblastic anemia in which the blood islands in the medullary portion of the bones are disturbed. Further interference with bony growth was observed in the provisional zones of calcification. These were thickened and in many areas reduplicated. The

TABLE 3.—*Results of First Gastric Analysis*

	Fasting	15 Minutes	30 Minutes	45 Minutes	60 Minutes
Total hydrochloric acid	13	17	22	23	23
Free hydrochloric acid	0	9	13	16	12
Blood	Small specs	Brownish	Brownish	Brownish	Brownish
Benzidene	4+	4+	4+	4+	4+
Mucus	4+	4+	4+	4+	4+
Lactic acid	0	0	0	0	0

width of the bone in this region was increased at the expense of the length, although the zones did not appear ragged. No evidence of rickets or scurvy was present. The spleen and the liver were enlarged. The roentgenologic findings indicated an alteration of the blood islands in the medullary portion of the bones, with changes from normal growth at the provisional zones of calcification. Further roentgenograms, taken two weeks after liver therapy was begun, revealed diminution in the size of the liver and the spleen. The long bones still showed a moderate degree of osteoporosis, but it was less marked than at the time of the original examination. The provisional zones of calcification were now much broader, with an appearance similar to that seen in healed rickets. The area spongiosa, which on the first plate showed almost a Trümmerfeld's zone, now exhibited evidence of new bone formation.

Second Admission: The urine was normal. Examination of the blood showed that nonprotein nitrogen, sugar, total cholesterol, cholesterol esters and calcium were present in normal amounts. A roentgen examination eight months after the first showed an almost complete restoration of the bones to normal. The length of the long bones had increased. The provisional zones of calcification, while still moderately thickened, more clearly showed the irregularity due to the previous interference with nutrition. The spleen and the liver were of normal size. The gastric analysis gave the results shown in table 4. (Inflammation of the upper respiratory tract was not present.) One-tenth milligram of histamine hydrochloride was injected during the test.

Microscopic examination showed the minimal amount of mucus and rare erythrocytes, leukocytes and round epithelial cells. Pus clumps were absent.

Summary.—A case of macrocytic hyperchromic anemia is reported. The history was that of disturbed gastro-intestinal function and dietary inadequacy. Gastric analysis revealed hypochlorhydria and evidence of inflammation. A high caloric, high vitamin diet and iron therapy resulted in but slight improvement. The addition of liver caused a specific response and rapid recovery. A gastric analysis five months after the first revealed that the inflammation previously noted was absent. The patient remained well for one year despite failure to take liver or meats regularly throughout that period.

COMMENT

The conception of primary macrocytic hyperchromic anemia as a syndrome conditioned by deficiency is now well established. The type includes the addisonian anemia, primary anemia of the tropics, sprue, Gee's disease, anemia of pregnancy and anemia accompanying parasitic infestation and organic lesions of the gastro-intestinal tract.[16]

TABLE 4.—*Second Gastric Analysis*

	Fasting	½ Hour	1 Hour	1½ Hours	2 Hours	2½ Hours	3 Hours	3½ Hours
Total hydrochloric acid	9.8	37.4	66.6	39	16	..	18	17.6
Free hydrochloric acid	0	17.6	49.6	13	0	..	0	0
Blood	Small specs	0	0	0	0	..	0	0
Benzidene	2+	0	0	0	0	..	0	0
Mucus	1+	0	0	0	0	..	0	0
Lactic acid	0	0	0	0	0	..	0	0

The relation of variations of intrinsic and extrinsic factors to the etiology of the various types has been shown by Castle[17] and many

16. (*a*) Parsons and Hawksley.[13a] (*b*) Birkeland.[14] (*c*) Castle, W. B., and Rhoads, C. P.: Aetiology and Treatment of Sprue in Porto Rico, Lancet **1**:1198 (June 4) 1932; (*d*) Observations on the Etiology and Treatment of Sprue in Puerto Rico, Tr. A. Am. Physicians **47**:245, 1932. (*e*) Strauss, M. B.: Rôle of Gastro-Intestinal Tract in Conditioning Deficiency Disease: Significance of Digestion and Absorption in Pernicious Anemia, Pellagra and "Alcoholic" and Other Forms of Polyneuritis, J. A. M. A. **103**:1 (July 7) 1934.

17. Castle, W. B.: Aetiological Relationship of Achylia Gastrica to Pernicious Anemia, Proc. Roy. Soc. Med. (Sect. Med.) **22**:58 (July) 1929; Observations on Etiologic Relationship of Achylia Gastrica to Pernicious Anemia: Effect of Administration to Patients with Pernicious Anemia of the Contents of the Normal Human Stomach Recovered After the Ingestion of Beef Muscle, Am. J. M. Sc. **178**:764 (Dec.) 1929. Castle, W. B., and Townsend, W. C.: Observations on the Etiologic Relationship of Achylia Gastrica to Pernicious Anemia: Effect of Administration to Patients with Pernicious Anemia of Beef Muscle After Incubation with Normal Gastric Juice, ibid. **178**:748 (Dec.) 1929. Castle, W. B.; Townsend, W. C., and Heath, C. W.: Further Observations on the Aetiological

(*Footnote continued on next page*)

others. These factors, whether extrinsic, intrinsic or a combination, may be lacking permanently—as in true pernicious anemia—or temporarily—as in anemia of the tropics or that associated with parasitic infestation or with pregnancy.[18] Absorption may be the process primarily involved.[19] Indeed, Strauss [16e] believes that in the temperate regions all forms of deficiency are conditioned much more frequently by difficulties in absorption due to a pathologic condition in the gastrointestinal tract than by dietary inadequacies. Vomiting and diarrhea may interfere seriously with proper absorption.[20] Inadequate storage of hematopoietic material in the liver is occasionally responsible for the appearance of macrocytic anemia.[21] The reports of Faber,[6] Castle and Rhoads [16c] and others have demonstrated that in many instances iron is lacking and must be given to prevent the occurrence of microcytic hypochromic anemia, which would appear with the use of liver therapy alone.

Probably no other anemia can be prevented as easily as that of infancy, whether primary or secondary. Since true addisonian pernicious anemia during that period has never been definitely established, all anemia occurring in patients under 1 year of age may be assumed to be basically nutritional. The tremendous value of prophylaxis at

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Relationship of Achylia Gastrica to Pernicious Anemia, Lancet **1**:1062 (May 17) 1930; Observations on Etiologic Relationship of Achylia Gastrica to Pernicious Anemia: Nature of Reaction Between Normal Human Gastric Juice and Beef Muscle Leading to Clinical Improvement and Increased Blood Formation Similar to Effect of Liver Feeding, Am. J. M. Sc. **180**:305 (Sept.) 1930.

18. Straus, M. B., and Castle, W. B.: (*a*) Studies of Anemia in Pregnancy: Etiologic Relationship of Gastric Secretory Defects and Dietary Deficiency to Hypochromic and Macrocytic (Pernicious) Anemias of Pregnancy and Treatment of These Conditions, Am. J. M. Sc. **185**:539 (April) 1933; (*b*) Aetiology and Treatment of Anaemia in Pregnancy, Lancet **1**:1198 (June 4) 1932.

19. Castle and Rhoads.[16e] Connery, J. E., and Goldwater, L. J.: Parenteral Use of Liver Extract in Treatment of Pernicious Anemia, J. A. M. A. **98**:1060 (March 26) 1932; Pernicious Anemia: A Conditioned Deficiency; Observations on the Effects of the Administration of Substance Rich in Vitamin B Complex, New England J. Med. **209**:446 (Aug. 31) 1933.

20. Parsons and Hawksley.[13a] Castle, W. B.; Heath, C. W., and Strauss, M. B.: Observations on the Etiologic Relationship of Achylia Gastrica to Pernicious Anemia: Biologic Assay of Gastric Secretion of Patients with Pernicious Anemia Having Free Hydrochloric Acid and That of Patients Without Anemia or with Hypochromic Anemia Having No Free Hydrochloric Acid, and of the Rôle of Intestinal Impermeability to Hematopoietic Substances in Pernicious Anemia, Am. J. M. Sc. **182**:741 (Dec.) 1931.

21. Goldhamer, S. M.: Liver Extract Therapy in Cirrhosis of the Liver: Relation of Liver Dysfunction to Nonstorage of "Anti-Anemic" Substance in Producing a Blood Picture Resembling Pernicious Anemia in a Patient Secreting Free Hydrochloric Acid, Arch. Int. Med. **53**:54 (Jan.) 1934.

once becomes apparent. An easily digestible diet with the proper caloric and a high vitamin content should be established as soon as possible. Moderate doses of iron may be added very beneficially when the patient is about 5 months of age because of the extremely common nutritional anemia [22] which begins at about that period. Such prophylaxis also seems advisable in cases of underfeeding and malnutrition, since these conditions are so likely to cause anemia. Finally, all infants with disturbances of the gastro-intestinal tract and of nutrition—of even moderate duration—should have the benefit of preventive administration of iron and hematopoietic stimulants to prevent anemia, which otherwise would probably occur.

In all instances of nutritional disturbance a varied, well balanced diet of high caloric and high vitamin content should be used as a basis to which may be added the substances determined by investigation to be lacking in each case.

The specific effect of liver therapy on pernicious anemia has been clearly demonstrated by many workers. It has been shown also that liver is just as effective in the treatment of macrocytic hyperchromic anemia due to tropical sprue,[16e] pregnancy,[18b] parasitic infestations,[16e] etc. Faber,[6] Gerbasi,[7] Ducas and Jacquet [8] and de la Torre [9] have demonstrated specific responses to liver in cases of macrocytic hyperchromic anemia in patients under 1 year of age.

Iron plays an important though not primary rôle in the treatment of macrocytic hyperchromic anemia. Many observers have found it necessary for a final cure. Minot and Castle [23] have found that liver causes the erythrocytes of many patients with pernicious anemia to outstrip the hemoglobin in improvement to such an extent that the red cells become hypochromic and the patients require iron to raise the hemoglobin content to normal. Castle and Rhoads [16e] have recorded similar findings in some of their cases of the macrocytic anemia of tropical sprue. While many patients with the macrocytic anemia of pregnancy may be cured with liver alone, some have been found to require iron in addition to secure a complete cure.[18b] Metabolism in connection with the utilization of iron is far from being fully understood. Indeed, the syndrome of "idiopathic" hypochromic anemia often

22. Mackay, H. M. M.: Anaemia in Infancy: Its Prevalence and Prevention, Arch. Dis. Childhood **3**:117 (June) 1928; Nutritional Anaemia in Infancy: Some Observations on a Common Deficiency Disease, Proc. Roy. Soc. Med. **22**:29 (Feb.) 1929. Lewis, M. S.: Iron and Copper in the Treatment of Anemia in Children, J. A. M. A. **96**:1135 (April 4) 1931.

23. Minot, G. R., and Castle, W. B.: The Interpretation of Reticulocyte Reactions: Their Value in Determining the Potency of Therapeutic Materials, Especially in Pernicious Anaemia, Lancet **2**:319 (Aug. 10) 1935.

resembles that of pernicious anemia so closely, even to the presence of atrophy of the papillae of the tongue and gastric acidity, that Minot [24] suggested an investigation of the possible relationship between iron and the vitamin B complex.

Transfusions seem very effective in the therapy of pernicious anemia in infancy. Cooley [2] used small transfusions to great advantage in the apparent permanent cure of the condition. However, because of the specific curative effect of liver, transfusions should be reserved for cases of emergency in which an immediate supply of oxygen carriers is necessary to preserve life.

In considering the case here reported, dietary deficiencies and difficulties in absorption must be borne in mind as possibly playing important rôles in the etiology of the anemia. The patient had evidently progressed normally until the age of 4½ months. At that time he had an attack of purulent otitis media and alimentary intoxication. The severe diarrhea and vomiting which followed persisted for ten weeks. Certainly during this period the infant was unable to retain significant amounts of food, and what he did not vomit he lost through the diarrhea. Gastritis was found on admission. Marriott [25] and others [26] have concurred that many cases demonstrate a distinct and intimate relationship between infection of the middle ear and of the mastoid and gastroenteritis. The possibility of a similar relationship in the case under discussion is well worth consideration. Regardless of how the gastritis originated, it is reasonable to suppose that its presence was a factor of importance in preventing digestion of the foodstuffs necessary for proper nutrition. Secondary to and superimposed on the gastrointestinal disturbances were dietary inadequacies. The patient existed on nothing but mixtures of modified milk throughout the greater part of this illness. Fruits, vegetables, and meat extractives were completely lacking from the diet. Apparently the main objective was quantity, not

24. Minot, G. R.: The Anemias of Nutritional Deficiency: Etiology, Diagnosis, Treatment and Prevention, J. A. M. A. **105**:1176 (Oct. 12) 1935.

25. Marriott, McK.: Further Observations Concerning Nature of Nutritional Disturbances, Laryngoscope **35**:592 (Aug.) 1925; Further Observations Concerning Nature of Nutritional Disturbances, Am. J. Dis. Child. **30**:577 (Oct.) 1925; Remote Results of Certain Focal Infections Occurring During Infancy and Childhood, South. M. J. **19**:157 (March) 1926.

26. Kahn, B. S.: Relation Between Infection of the Upper Respiratory Tract and Gastro-Intestinal Infection in Infants, with Special Reference to the Rôle of Bacillus Morgani I, Am. J. Dis. Child. **49**:939 (April) 1935. Carmack, J. W.: Mastoiditis with Gastro-Intestinal Disturbance in Infants, Tr. Am. Laryng., Rhin. & Otol. Soc. **36**:426, 1930. Mitchell, A. G.; McCarthy, M. F.; Leichliter, J. W., and Seinsheimer, F.: Otitis Media and Its Relation to Gastro-Enteritis, J. A. M. A. **92**:970 (March 23) 1929.

quality or type, of food. It might be pointed out here that when the infant recovered from the deficiency state he maintained his nutritional reestablishment and continued to make further progress on a diet devoid of meat in any form. Evidently his diet between admissions was adequate for continued growth and development. However, not only were dietary conditions corrected, but absorption difficulties vanished while the patient was in the hospital and did not reappear during the interim. Vomiting and diarrhea were never present. Gastric analysis during the second hospitalization showed the practical absence of the previously observed gastritis.

During his first hospitalization the patient was found to be secreting an abnormally small amount of hydrochloric acid in his stomach. Concomitantly with his general improvement the amount of hydrochloric acid reverted to normal. This finding was reported in a similar type of anemia occurring in pregnant women.[18a] Gastric analysis was done in only two of the seventeen cases of macrocytic hyperchromic anemia reported.[6] In both instances the value for gastric hydrochloric acid was abnormally low. Gastric hypochlorhydria may thus be a finding characteristic of this anemia, as of many similar anemias.

During treatment it was observed that the high caloric and concentrated vitamin diet had practically no demonstrable effect per se. The addition of iron seemed to be effective clinically but less so hematologically. There was a definite reduction in the size of both the liver and the spleen. However, the diminution was moderate and limited. No gain in weight occurred throughout the administration of iron. The improvement in the blood picture was minimal, more marked in the hemoglobin than in the erythrocytes, and the color index remained above 1. There was no demonstrable effect on reticulocyte production, but the nucleated red blood cells disappeared rapidly and never reappeared. The bone marrow showed stimulation by temporarily pouring into the blood stream large numbers of immature granulocytes.

The probable specific effect of liver therapy was evident both clinically and in the blood picture. Within one week after it was instituted the infant appeared much brighter and began to gain weight and generally to improve. The effect on weight was remarkable. At the time of the patient's admission and throughout the four weeks of iron therapy the diet had been of high caloric value, about 66 to 67 calories per pound (0.45 Kg.). At no time had there been any significant gain in weight. With the administration of liver extract the child began to gain weight with phenomenal rapidity, averaging from 7 to 19 ounces (198.45 to 538.65 Gm.) per week. While his weight increased his energy quotient rapidly diminished because his total caloric intake was maintained at the same level. At the time of discharge from the hos-

pital the energy quotient was 44. In spite of the rapid decline of caloric intake per pound, the infant's rate of gain increased during the latter weeks of his stay. It seems highly improbable that the extract of 50 Gm. of liver daily could of itself supply sufficient nourishment more than to compensate for the diminishing energy quotient and accomplish the gain in weight observed. Further, the effect of the liver extract persisted for at least five months, because at the termination of that period (on the second admission to the hospital) it was found that the patient had gained 7 pounds (3,175.14 Gm.) on a regular meat-free, liver-free diet.

The generalized effect of the liver therapy was just as striking and definite. By the time the patient was first discharged his liver and spleen had diminished to a point where they were barely palpable. At his readmission they could not be felt. The roentgenogram taken at that time showed the previously described diaphyseal reduplication to be healing rapidly. It certainly seems that a generalized nutritional deficiency of multiform manifestations had continued to respond definitely to the liver therapy originally given. This fact is even more impressive when one recalls that the continued gains were made on a diet of sufficient quantity and quality with the exception that it did not contain liver or other meats.

On the blood picture the effect was typical of the action of liver extract in any type of macrocytic hyperchromic anemia. On the fourth day after liver therapy was initiated the reticulocyte count had risen from 3.4 to 8.4 per cent. One cannot estimate how near maximal the effect of the therapy was, since the initial level of the red blood cells was above 3,000,000.[23] At any rate, the effect was definite and real. Eighteen days after the administration of liver extract was begun the reticulocytes attained a normal level and remained there. The erythrocytes responded markedly, climbing very much more rapidly than the hemoglobin to the normal value and remaining there. The color index fell below 1 and remained at that level. The complete return to normal persisted for at least one year, as evidenced by the blood pictures seen at the time of the second admission and by the later routine health examination. No noteworthy alteration in the leukocytic picture occurred except that the moderate lymphocytosis present in the later stages of the period of iron therapy disappeared, and the white blood cells attained their normal relationships.

SUMMARY AND CONCLUSIONS

A case of macrocytic hyperchromic anemia in an infant under 1 year of age is reported.

The various etiologic factors concerned are briefly discussed.

The presence of diminished gastric secretion of hydrochloric acid in this type of anemia is shown and the need of gastric analysis stated.

The specific effect of liver extract and the nonspecific effect of iron are demonstrated.

The absence of relapse after one year without antianemic therapy is noted.

The literature concerning the condition is reviewed.

The value of prophylaxis is emphasized.

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Progress in Pediatrics

INTRACRANIAL HEMORRHAGE OF THE NEW-BORN

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Perhaps I should apologize for discussing a condition which has been so thoroughly treated by various writers. However, I have two reasons for choosing this subject. First, owing largely to some statistics brought out at the White House Conference on Child Health and Protection and widely disseminated, there has been a large popular interest in intracranial hemorrhage of the new-born: an interest which has been associated with a great deal of criticism of the medical profession. Second, I think it is frequently wise to review a subject critically though it may have received a great deal of attention, since often its exposition has followed beaten paths, which may or may not lead to rational conclusions.

It is my intention not to attempt to discuss the entire subject of intracranial hemorrhage but to pick out certain phases which seem to me most worthy of consideration. I shall discuss first the frequency of intracranial hemorrhage of the new-born and shall attempt to bring out certain causes for the differences in statistics. In examining statistics concerning the new-born it is extremely hard to find any which will bear the light of criticism. Perhaps in the future one of the barriers to a just consideration of the subject will be removed, since for the last few years a large proportion of women have been delivered in hospitals whether the labor was normal or not. In the past obstetric care in normal deliveries was practiced largely in the home, and it was only when some complication developed that the woman was rushed to the hospital. Again, hospital care has frequently meant care by experts, while home care has often meant the employment of a physician who had no special training in obstetrics. There have been styles in obstetric methods as there have been styles in dress. In obstetrics as in other branches of medicine men have run to hobbies, so that one cannot generalize as a rule from statistics in this field.

Tables 1 and 2 give some idea of the relative frequency of intracranial hemorrhage. In the first table, that of Gillespie,[1] which is con-

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1. Gillespie, J. B.: Stillbirths: Analysis of the Causes of Death in Three Hundred and Thirty-Eight Cases as Determined by Necropsy, Am. J. Dis. Child. **44**:9 (July) 1932.

cerned with stillbirth, one notes that trauma at birth constitutes the cause in almost 30 per cent of the cases. In this connection, trauma at birth as a cause of death is principally represented by intracranial hemorrhage. In the second table, that of Holt and Babbitt,[2] accidents of labor, which probably, as in the series of cases studied by Gillespie,

TABLE 1 (Gillespie).—*Causes of Death in 338 Cases of Stillbirth*

Cause of Death	Males	Females	Total	Percentage	Age						
					Less Than 5 Months	5-6 Months	6-7 Months	7-8 Months	8-9 Months	9-10 Months	10 Months and More	Unknown
Stillbirth	180	158	338	....	1	10	36	42	43	59	101	46
Syphilis	11	7	18	5.32	..	..	1	3	4	7	..	3
Toxemia of pregnancy	6	9	15	4.42	..	..	1	4	3	3	3	1
Placenta praevia	4	7	11	3.25	..	..	..	..	3	2	5	1
Abruptio placentae	9	3	12	3.55	..	..	..	2	1	4	4	1
Prolapse and compression of cord	4	5	9	2.66	..	..	1	..	1	3	4	..
Prematurity	33	21	54	15.97	1	3	16	12	12	2	..	8
Past maturity	2	2	4	1.18	..	..	..	..	..	..	4	..
Trauma at birth	54	47	101	29.88	..	1	5	5	8	18	61	3
Malformation (congenital)	15	22	37	10.94	..	1	8	7	5	5	3	8
Vaginal bleeding (cause unknown)	2	2	4	1.18	..	..	2	..	..	1	..	1
Difficult labor (cause not given)	..	2	2	0.59	..	..	..	..	..	1	1	..
Asphyxia (cause undetermined)	1	..	1	0.29	..	..	..	..	..	1	..	..
Meningitis (focal)	..	1	1	0.29	..	..	..	..	..	1	..	..
Fetus papyraceous	..	1	1	0.29	..	..	..	..	..	..	..	1
Oligohydramnios	1	..	1	0.29	..	..	..	1	..	..	..	..
Intra-uterine death (macerated)	31	23	54	15.97	..	5	2	7	6	9	9	16
Undetermined	7	6	13	3.84	..	..	..	1	..	2	7	3

TABLE 2 (Holt and Babbitt).—*Causes of Death During First Fourteen Days*

Cause of Death	Under 1 Day		Under 7 Days		7 to 14 Days		Total in 14 Days		Grand Total
	Premature	Full Term	Premature	Full Term	Premature	Full Term	Premature	Full Term	
Congenital weakness	93	2	120	7	14	2	134	9	143
Accidents of labor	1	14	1	32	..	..	1	32	33
Pneumonia	..	..	3	9	3	13	6	22	28
Atelectasis	3	7	3	14	1	7	4	21	25
Congenital spyhilis	5	0	6	1	6	0	12	1	13
Malformation	..	4	2	7	0	3	2	10	12
Hemorrhage	..	..	..	8	..	2	..	10	10
Sepsis	..	..	..	2	..	7	..	9	9
Asphyxia	..	7	..	8	..	..	..	8	8
Accidental	..	1	..	2	..	..	..	2	2
Undetermined	..	3	..	8	..	..	..	8	8
Total	102	38	135	98	24	34	159	132	291

consist largely of instances of intracranial hemorrhage, represent the cause of death of 33, or about 11 per cent, of the infants who died

2. Holt, L. E., and Babbitt, E. C.: Institutional Mortality of the New-Born: A Report on Ten Thousand Consecutive Births at the Sloane Hospital for Women, New York, J. A. M. A. **64**:287 (Jan. 23) 1915.

shortly after birth. It should be said in connection with this group that the children were born in a well regulated hospital and that in each instance labor was attended by a well trained obstetrician.

Perhaps this has some significance, for if one turns to other statistics, for instance those of Adair,[3] one finds tabulated the abnormalities noted at autopsy in 961 instances of stillbirth and neonatal death, of which the largest single cause was trauma at birth, which accounted for 300, or 31.2 per cent. This figure approximates closely that of Gillespie for stillbirths. Adair's investigation was made from a rather extensive area, the autopsies having been made at the medical school of the University of Minnesota, but these autopsies were performed on babies a large proportion of whom had been born outside the hospital. According to the statement, the "cases were secured from various hospitals and from private practitioners." This is of importance, since it is possible that the figures obtained from the Sloane Maternity Hospital therefore represent a difference of results according to the type of attention given. One cannot, however, draw this conclusion off hand, and more will be said later in regard to it.

It would seem from other statistics that the figures of Gillespie and of Adair are not too high. It is interesting to note that Clein [4] found that in the group of premature infants studied by him the cause of death of 50 per cent of those who died was cerebral hemorrhage. Irving,[5] reporting from the Boston Lying-In Hospital, stated that there were 99 cases in which the condition was diagnosed as intracranial hemorrhage among 13,849 deliveries between 1909 and 1929. There were 182 autopsies which included examination of the head, and of these, 73, or 40 per cent, revealed intracranial hemorrhage. Fleming [6] noted cranial injuries in 350 of 8,000 infants delivered alive at the Royal Maternity Hospital in Glasgow. It is evident, therefore, that between 25 and 40 per cent of the deaths of the new-born may be attributed to intracranial hemorrhage and that the number of instances of intracranial hemorrhage in maternity hospitals varies with the hospital but the condition is probably as frequent as 1 to 25 or as low as 1 to 150 deliveries.

The reason that the medical profession has not been sufficiently impressed by these figures is that most newly born infants are normal. This is such an unusual thing for hospital patients that the deformed, injured or diseased infant is regarded as a rarity. If one should estimate the number of deaths in the population at large from any disease

3. Adair, F. L.: J. Michigan M. Soc. **31**:363 (June) 1932.

4. Clein, Norman W.: Premature Infants: A Clinical and Pathologic Study, Am. J. Dis. Child. **37**:751 (April) 1929.

5. Irving, F. C.: New England J. Med. **203**:499, 1930.

6. Fleming, G. B.: Lancet **2**:532, 1931.

or type of injury, one would be appalled to find that it occurred as frequently as once in every 150 persons. Therefore, not only from the standpoint of the proportion of deaths due to intracranial hemorrhage but also on account of its actual frequency the condition assumes paramount importance.

That conservative obstetric procedures may be an important factor seems to be suggested by table 3, for which the data were taken from the outpatient obstetric service of the Central Free Dispensary, in Chicago, which is operated in connection with the Rush Medical College. The normal infants are attended in their homes by medical students under the supervision of an intern, and those with pathologic conditions are taken to the Presbyterian Hospital. The instructions to the students are such as to assure the greatest conservatism. So far as I am able to determine, this is a record of all infants delivered by that service during the years in question, and practically all the infants who died or were stillborn had postmortem examinations. From this table it may be seen that only 1 of 226 stillborn infants showed intracranial hemorrhage and that of 166 new-born infants who died only 20, or 12 per cent, showed intracranial hemorrhage. Thus, statistics compiled from records from an institution in which one may reasonably expect obstetric care to be of a conservative nature show a difference of between 10 and 15 per cent from those ordinarily quoted. It therefore seems not unlikely that the method of delivery and the attitude of the accoucheur have a definite influence on the rate of mortality from intracranial hemorrhage.

One thing that must always be remembered regarding intracranial hemorrhage of the new-born—I think that some of the things I have to say later will stress this even more significantly—is that one can make no estimate of the number of instances of intracranial hemorrhage unless the brain has been seen either at autopsy or at operation and unless certain cases are included in which the condition is diagnosed in later life from paralyses. Even in this realm the determination of a previous intracranial hemorrhage is extremely hard.

Before I conclude these statements regarding etiology, I must make the broad generalization that no matter how much the mortality from intracranial hemorrhage may be due to radical obstetric methods, in a given case the result must depend on the judgment of the individual physician. It is altogether conceivable that in many instances intracranial hemorrhage can be prevented by proper obstetric procedure, or rather by intervention at the proper time, and from the occurrence of intracranial hemorrhage in infants delivered by perfectly normal labor and by cesarean section it is known that in many cases the condition is on the basis of intra-uterine trauma.

TABLE 3.—*Causes of Death of Infants Delivered by the Outpatient Obstetric Service of the Central Free Dispensary, Chicago*

	1921	1922	1923	1924	1925	1926	1927	1928	1929	1930	1931	1932	Total	Percentage
Number of cases	760	745	627	772	753	787	821	827	676	736	971	1,489	9,964	
Deaths, maternal	1	1	3	3	2	2	2	2	1	1	1	2	21	0.205
Cause of death	Heart disease	Pneumonia	Heart disease; pneumonia; placenta praevia	Hemorrhage; heart disease; pneumonia; placenta praevia	Pneumonia; labor and anesthesia	Heart disease; eclampsia	Puerperal sepsis; eclampsia	Puerperal sepsis; labor and anesthesia	Diabetic coma	Eclampsia	Shock and collapse	Respiratory failure; retroplacental hemorrhage		
Births	760	745	627	772	753	787	821	827	676	736	986	1,501	9,991	*
Stillbirths	17	19	14	29	21	20	18	19	13	14	17	25	226	2.26
Maceration	6	6	3	17	10	11	9	10	6	8	5	9	100	40
Prematurity	6	4	1	1	3	3	4	3	1	2	1	4	33	13
Asphyxia	3	8	7	9	8	6	5	5	6	4	6	7	74	32.75
Congenital defects	2	1	3	2	0	0	0	0	...	...	4	1	13	5
Congenital syphilis	...	...	...	...	...	...	...	1	...	...	1	...	2	
Pulmonary atelectasis	...	...	...	...	...	...	...	...	...	...	...	3	3	
Intracranial hemorrhage	...	...	...	...	...	...	...	...	...	...	...	1	1	
Neonatal deaths	15	13	9	14	15	18	15	23	11	8	10	15	166	1.66
Prematurity	3	5	5	5	5	8	9	14	6	5	3	4	72	43.4
Asphyxia	3	2	...	3	...	3	1	6	...	...	...	...	18	10.9
Intracranial hemorrhage	1	2	1	2	2	3	3	1	1	...	2	2	20	12
Hemorrhagic disease	2	1	1	2	1	1	...	...	...	...	2	1	11	6.6
Congenital defects	5	1	...	2	4	1	2	...	3	3	1	6	28	18.1
Pneumonia	1	...	1	...	...	...	...	1	...	...	...	1	4	2.4
Sepsis	...	...	...	...	...	...	...	...	1	...	...	...	1	0.6
Syphilis	...	...	...	...	3	1	...	1	...	...	2	...	7	4.2
Other causes	...	2†	1‡	...	...	1§	...	...	...	...	...	1‖	5	3.0

* Percentage is not accurate for 1921 to 1930 inclusive.
† Apnea; nephritis.
‡ Edema of larynx.
§ Dehydration.
‖ Air embolism in coronary artery.

In speaking of the evaluation of statistics concerning mortality from this condition, I have just said that diagnosis must be based almost entirely on postmortem examination. There are many who will dispute this statement. They will say that the diagnosis of intracranial hemorrhage intra vitam is comparatively easy and that a lumbar or cisternal puncture will reveal the facts in the case. My experience with lumbar puncture as a means of diagnosis of intracranial hemorrhage has not been happy. It has led me to make some rather dogmatic statements. The presence of blood in the spinal fluid is not a definite indication of intracranial hemorrhage as I understand it. That it may be an indication of an occasional small petechial hemorrhage or that it may mean venous congestion, with some passage of red cells through the vessel walls, I do not question, but I have repeatedly seen infants go to autopsy in whom, in spite of the presence of blood in the spinal fluid, which was usually taken by lumbar puncture, no hemorrhage of any size or of any consequence was found. If one stops to interpret this, one will see that there is no reason for believing that blood in the spinal fluid necessarily means intracranial hemorrhage. There are many pitfalls. The venous plexus in the walls of the spinal canal in the new-born is extremely rich, and the vertebral bodies are almost cavernous with venous sinuses. Puncture of a blood vessel or sliding the needle into the vertebral body is comparatively easy and results in a bloody fluid, or, because of the loose attachment of the dura to the vertebral column at this age, if the needle is not sharp, one can push the membrane ahead of it and produce a pocket which soon fills with blood. With cisternal puncture there are not these dangers; yet I have recently had evidence that cisternal puncture too may go wrong. I am convinced from my experience that blood in the spinal fluid is frequently the result of marked congestion or perhaps of fine petechial hemorrhages and that the blood present under those circumstances is frequently not small in amount. The evidence of this is not only pathologic but clinical.

However, if one wishes to draw conclusions from the material obtained by lumbar puncture, there are three things that are necessary: first, that no puncture, successful or otherwise, shall have preceded the one by which the material is obtained; second, that the red cells, if present, shall have undergone degeneration, and, third, that definite xanthochromia (Levinson, Greengard and Lifvendahl [7]) shall be present. The third is not so important because often one will get a perfectly clear but xanthochromic spinal fluid. Levinson and his associates have shown that this xanthochromic fluid may be neither bile nor blood, since the benzidine test and the van den Bergh test give negative results

7. Levinson, A.; Greengard, J., and Lifvendahl, R.: Cerebrospinal Fluid in the New Born, Am. J. Dis. Child. **32**:208 (Aug.) 1926.

in some cases. They concluded: "Fresh blood in the spinal fluid is often the result of trauma as well as of intracranial hemorrhage."

However, if physicians are really to know the frequency of intracranial hemorrhage, it will be necessary for them to depend on statistics not only concerning patients who come to autopsy but also concerning those who have shown definite clinical evidence of the presence of hemorrhage. By examining the cerebrospinal fluid of premature infants and comparing the results with observations made at necropsy, Glaser [8] found that of 26 instances in which evidence of cerebral hemorrhage was present at necropsy the spinal fluid was bloody in 19 and clear in 7. Small petechial hemorrhages were not classified as cerebral hemorrhages. Of 42 instances in which evidence of cerebral hemorrhage was not noted at necropsy, the spinal fluid was grossly bloody or hazy in 13 and clear in 29. In a subsequent report [9] he listed 9 cases of meningeal hemorrhage or acute meningeal congestion in which there was bloody fluid and none in which there was clear fluid. On the other hand, of 14 infants with no meningeal hemorrhage or acute meningeal congestion, 2 had bloody fluid and 12 had clear fluid. In this second group the patients with cerebral hemorrhage were not separated from those with cerebral congestion. From a practical standpoint this is important, because recovery from cerebral congestion takes place readily, while cerebral hemorrhage almost always leaves a damaged brain. Of the total number (68) of infants examined in Glaser's first study, 20, or about one fourth, had abnormalities of the cerebrospinal fluid which were distinctly misleading. So large an error for such a procedure shows it to be of questionable value. It is therefore exceedingly important to approach the subject of diagnosis not only from the standpoint of proposed treatment but also from that of incidence of the condition.

If one consults the average textbook, one is impressed by the fact that the diagnosis of intracranial hemorrhage is easy and that this diagnosis is based usually on two things—convulsions and blood in the spinal fluid. With the latter as a basis for diagnosis I have already taken issue. What about convulsive seizures? It is well known that many conditions in the new-born produce convulsive seizures and that the pathologic changes in these conditions may or may not be confined to the cranial cavity. It would therefore seem wise to consider the

8. Glaser, Jerome: The Cerebrospinal Fluid of Premature Infants, with Special Reference to Intracranial Hemorrhage and Pigmentation, Am. J. Dis. Child. **36**:195 (Aug.) 1928.

9. Glaser, Jerome: Cerebrospinal Fluid of Premature Infants: Results of a Series of Spinal Punctures in One Hundred and Seventy Cases, with Special Reference to the Origin of Physiologic Xanthochromia in the New-Born Infant, Am. J. Dis. Child. **40**:741 (Nov.) 1930.

various causes of convulsive seizures in those children who survive and not only in those who die. Even in the latter group I have frequently been amazed by my failures.

In considering the causes of convulsive seizures in the new-born, one must remember that these include anything which may produce cerebral irritation. This means almost every disease which affects the infant at this age. This cannot be too strongly emphasized, since there is a marked tendency to regard convulsions as sufficient evidence for a diagnosis of intracranial hemorrhage. One may divide the conditions which are to be considered for this purpose into two main groups: first, those in which there is no evidence of intracranial lesion and, second, those in which such a lesion is known to exist. In the first group must be included practically all the febrile diseases, since any one of these is likely to produce convulsive seizures or at least muscular twitchings. In some instances this may be due to cerebral congestion. In others it is unquestionably the result of some deficiency in the metabolism. It is unnecessary here to stress unduly the incidence of such conditions as sepsis of the new-born, erythroblastosis of the new-born and the various infections, such as pneumonia and pyelitis, as causes of this symptom. It is well known that any of these conditions may produce it, and with proper care it should be possible in the majority of instances to determine these. There is always a possibility, however, that some intracranial lesion is associated with these diseases.

In this connection one should recognize the existence of tetany of the new-born. Of late this has received a great deal of attention, although I have not had the fortune to observe a case. From reports, however, tetany of the new-born seems to differ from that of older infants in that the premonitory symptoms, such as laryngismus stridulus and carpopedal spasm, are not encountered. The condition, however, is associated with a decrease in the amount of calcium in the blood. That this is always true has been disputed by some. There should be a hint in the history of the mother that would lead one to suspect the presence of such a condition in the child, but apparently from reports this is not often the case. This condition too can be readily eliminated, for the danger, as is so frequently the case in the new-born, is that physicians do not make exhaustive attempts to find out the various possibilities but are likely to jump to conclusions.

Of metabolic disturbances, the one which is probably most frequent is that which has been described by Marriott and Hartmann [10] under the title "Hypoglycemia." That this condition is met with in the new-born has been conclusively proved by them; that in many instances

10. Marriott, W. McK., and Hartmann: Paper read at the meeting of the American Academy of Pediatrics, Regions II and III, St. Louis, Nov. 18 and 19, 1935.

convulsive seizures are present and that death may occur without other known cause have also been shown. If it is thought of, the presence of this condition can be readily ascertained by determination of the blood sugar, the value for which is nearly always below 50 mg., sometimes as low as 20 mg., per hundred cubic centimeters. Children with this condition are usually the offspring of diabetic mothers, and under such circumstances there is definite indication for the determination of blood sugar.

It is also true that changes in the blood supply to the brain may be responsible for the occasional association of convulsive seizures with congenital cardiac lesions without any evidence of cerebral lesion. Many years ago I saw a baby who had not only generalized convulsions but also unilateral sweating. There was no evidence that I could determine of involvement of the heart, and without reservation I made a diagnosis of intracranial hemorrhage. The condition was so severe that I had no hesitancy in predicting a fatal outcome. In one respect at least I was correct. The child died. But much to my surprise and to the surprise of all who had observed this patient, there were no lesions in the brain but a severe malformation of the heart. I have seen one child since then in whom I suspected that the same conditions were present.

If one turns from those conditions producing convulsions in infancy which are not associated with cerebral lesions to those in which such lesions are present, one is confronted by even greater difficulties in diagnosis than with the former group. It is comparatively easy to diagnose meningitis. The patient rarely shows symptoms before the third day, and the condition is usually accompanied by bulging of the fontanel and symptoms other than convulsions pointing to meningeal irritation. A lumbar puncture, whether the fluid contains blood or not, will usually reveal the nature of the condition.

A second condition which is far more frequent is that designated as congestion, edema or sterile meningitis, the nature of which seems to be obscure, as evidenced by the various names which are given it. However, that as a result of trauma at birth congestion and edema of the brain occur in a certain number of children is self-evident. Waitz[11] characterized the resulting condition as sterile meningitis and brought evidence to show that the descriptive name is correct. From a practical standpoint it makes little difference whether one regards this condition simply as congestion with edema or as congestion with edema and sterile meningitis. That a difference between the symptoms of this condition and those of intracranial hemorrhage exists has never been proved.

11. Waitz, Robert: Les lésions cérébro-meningées à la naissance, Paris, Gaston Doin, 1931.

That the severity of the symptoms may be less is generally conceded. In this condition more than in any other the diagnostic value of lumbar puncture would seem to be apparent, and yet it signally fails. As previously mentioned, Glaser, after a study of the results of lumbar puncture in the premature infant, grouped the two conditions under one heading. That failure in diagnosis is rather frequent may be strongly suspected. In fact, it seems to me that when a child recovers from symptoms due to a cerebral lesion the nature of which has not been determined, the burden of proof rests with him who claims that the condition is an intracranial hemorrhage instead of edema.

Some fifteen years ago I was asked to see the new-born son of one of my medical colleagues. Three other physicians were in attendance at the time, all of whom had had considerable experience with infants of this age. The child was deeply cyanotic, and had convulsive twitching periodically, with generalized convulsive seizures at intervals. We agreed that he had had an intracranial hemorrhage. The others wished to do a lumbar puncture, but I prevailed on them not to, since I felt that any such procedure would tend to increase the hemorrhage and would not be of either diagnostic or therapeutic value in that case. They finally decided that my point of view was correct, and he was allowed to go without further treatment other than supportive measures. He is now in military school. Since the first week of life he has had but one convulsive seizure, which occurred during an acute febrile attack when he was 18 months of age. His father says that he is doing poorly in mathematics but that if memory serves him correctly that deficiency is inherited and not acquired. Did this boy have an intracranial hemorrhage? I think not. What he must have had, to my way of reasoning, is severe congestion and edema. Any physician who has had much to do with newly born infants must have had many experiences such as this. It is not the only one which I have had, but I am sure it is the most striking.

In the question of differentiation between intracranial hemorrhage and edema, the observations of Waitz on the cellular elements of the spinal fluid are most interesting. In those cases described by him as instances of aseptic meningitis of the new-born there was hypersecretion as well as edema, the edema being primary and the hypersecretion secondary. The maximum amount of fluid was obtained from the third to the fifth day, and the number of cells in the fluid decreased gradually with the amelioration of symptoms. The albumin gradually disappeared. Leukocytes were present, as were plasmocytes and endothelial cells; the endothelial cells frequently engulfed portions of red cells. Large cells which he termed hematomacrophages frequently engulfed entire red cells. By the fifteenth to the twentieth day the spinal fluid had cleared entirely. It is to be remembered that by means of injection

Waitz practically embalmed the brain and its coverings in a solution of formaldehyde before the skull was opened. He allowed the brain to remain in situ for five days before the autopsy was completed. Even if the observations of Waitz are correct, and I presume that they are, it would be rather hard to see how such observations would help materially in the differentiation of the two conditions.

Rydberg [12] in an exhaustive study of intracranial hemorrhage came to the conclusion that the ocular symptoms are of peculiar importance and that the pupillary disturbance may even indicate the location of the lesion. Other symptoms point to intracranial trouble but not to intracranial hemorrhage.

There is still another intracranial lesion which is all too common and which may at times produce convulsive seizures. Little consideration has been given to the various defects of the brain of a congenital nature as a cause of such convulsive seizures. In this respect the following case seems to me to be especially interesting.

Case 1.—M. B., a white boy aged 6 months, entered the Presbyterian Hospital on July 2, 1935, in the service of Dr. Parmelee. The child was born by normal delivery at full term, with a birth weight of 9¼ pounds (4,195 Gm.). On the day of birth he had several generalized convulsions, and these persisted for a week. At that time the diagnosis of intracranial hemorrhage was made, and he was given two intramuscular injections of blood. The history was that he had not cried except once during the first two weeks of life—on the tenth day—and that he had a shrill, weak cry. He did not nurse well but gradually improved and went along nicely until the third month, when there began to be twitchings on the right side, which became general. At the time of entrance he was having each day at least one attack which lasted for fifteen minutes. There was no cyanosis. The family history was entirely irrelevant, and this was the first child. He had been fed artificially on a well regulated diet. He had had no contagious disease or any other illness save those noted.

The weight at the time of his entrance into the hospital was 16 pounds and 5 ounces (7,399 Gm.). The patient was well nourished, and the examination gave essentially negative results throughout, except for large tonsils and a peculiar configuration of the head which was 17 inches (44 cm.) in circumference and definitely dolichocephalic, with a keel-shaped deformity of the frontal region. The sagittal and frontal sutures were represented by definite ridges. The eyes reacted to light, but he could not hold up his head and was evidently idiotic. The blood and the urine were normal. The Wassermann reaction was negative. The calcium content of the serum was 12.7 mg. per hundred cubic centimeters and the phosphorus content 6.7 mg. The spinal fluid was clear, with a slight increase of pressure; 9 white cells and many red cells were present; the culture gave negative results.

The roentgenograms of the long bones showed no abnormality. The abnormalities of the skull can best be seen in the encephalograms (fig. 1). Both ventricles were filled to large size; the left was apparently slightly larger than the right.

12. Rydberg, Erik: Cerebral Injury in New-Born Children Consequent on Birth-Trauma, New York, G. E. Stechert & Company, 1932.

A small amount of air had escaped into the posterior parietal region and was present in large irregular masses. The anteroposterior views show that most of this air was on the right side and toward the periphery. Roentgenograms taken after a few hours showed a good deal of air out of the ventricles, the greatest amount remaining on the left and being irregularly distributed in both parietal regions. In addition, the skull was small, with evidence of an encysted cephalhematoma (bone cyst) in the right parietal region.

It is rather interesting that when the roentgenogram was taken with the head downward (fig. 2) there was a shift of the air to the region of the base of the skull, especially in the posterior fossa. It is evident that I had to deal with agenesis or hypoplasia of the brain. The question arises, of course, whether a child could have such an extensive hemorrhage as this and live. It seems to me that the most interesting evidence is that which is given by a roentgenogram which was taken of the child in utero (fig. 3). This shows that before birth the anterior fon-

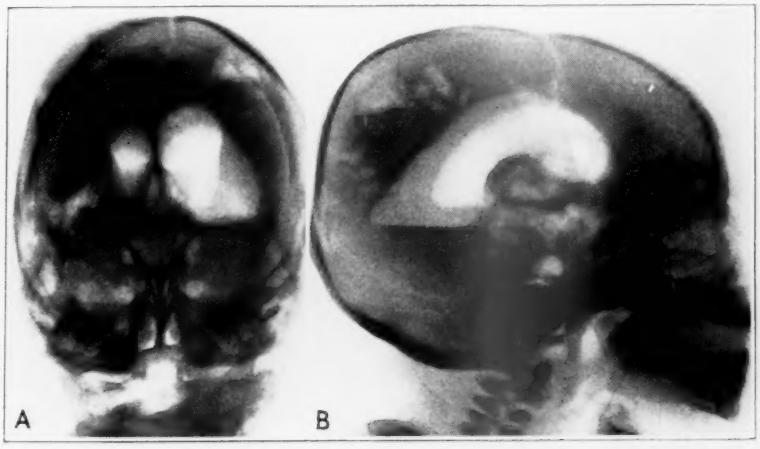

Fig. 1.—*A*, anteroposterior view of the head, showing both ventricles dilated, the left larger than the right. Air is present in the left parietal region, and an encysted cephalhematoma is present. *B*, lateral view of the head, showing the same condition.

tanel was closed and the frontal region of the skull appeared to be keel shaped.

In this case there was obviously a massive defect of the brain associated with distention of the ventricles, presumably from hydrocephalus. Such a condition is probably far more frequent than physicians realize or care to admit. They repeatedly see children with mental or physical defects which are attributed to intracranial hemorrhage of the newborn. It has always been rather hard for me to visualize a hemorrhage which would produce the lesion which the physical examination suggests. In the case just cited the diagnosis was intracranial hemorrhage of the

new-born, but I think the evidence is plain enough that the condition existed previous to birth and that it was in reality agenesis of the brain rather than a lesion produced by intracranial hemorrhage. It is interest-

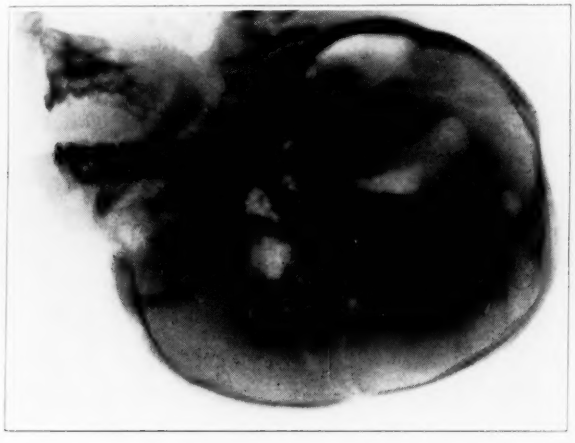

Fig. 2.—Encephalogram of the skull with the head downward, showing the accumulation of air in the occipital fossa.

Fig. 3.—Roentgenogram of the head before delivery, showing closed fontanels and a scaphoid deformity in the frontal region.

ing, in view of the fact that this opinion is so widespread, to note the decision arrived at by neurologists after a thorough investigation of the subject. The condition is usually associated with various kinds of

central paralysis, often diplegia, and it is in connection with this condition that the neurologists have expressed opinions. Freud,[13] in speaking of infantile cerebral paralysis, stated: "Since such injuries (birth trauma with meningeal hemorrhage) are so frequently without any effect, one cannot exclude the possibility that the existent diplegia is congenitally conditioned in spite of Little's case histories and that in certain cases the difficult labor itself is only a manifestation of a deeper lying influence which has dominated the development of the fetus or the organism of the mother."

In 1924 Collier[14] stated conclusively that after a thorough review of Little's report on diplegia he could find no evidence that Little in any case attributed the condition to intracranial hemorrhage of the new-born. In his masterly address on the pathogenesis of cerebral diplegia before the neurologic section of the Royal Society of Medicine, Collier went deeply into the question of the association of intracranial hemorrhage of the new-born with diplegia or with Little's disease. He called attention to the generally accepted notion that diplegia is frequently the result of such a hemorrhage. After going carefully into the literature on the subject he found absolutely no evidence that such is the case and ended his discussion of this portion of the subject with the following statement: "The evidence demands the verdict that meningeal hemorrhage should be deleted as a causal factor of any infantile spastic state."

Ford,[15] who made a careful study of cerebral palsies, found that only 6 per cent of those studied were due to injury at birth. He stated: "Common, diffuse, meningeal hemorrhage which is not large enough to cause death, apparently leaves no residuum in an overwhelming majority of cases. The real birth injuries to the brain are caused by the irregular intracranial hemorrhages and necroses, by depressed fractures with laceration of the brain and undoubtedly by more or less encapsulated meningeal hematomas which compress and soften the cortex." He stated too that the diplegia is "the result of a physiological process of intra-uterine origin" and is not due to meningeal hemorrhage at birth.

With all this evidence that such paralyses are not the result of intracranial hemorrhage, why does one continually meet with the statement that such and such a condition, either of mental defect or of central paralysis, is caused by hemorrhage into the brain at the time of birth? It seems to me that this is largely due to the fact that the wish is father to the thought. For some reason there is a tradition that mental defect in the offspring carries with it family disgrace and that if one may attribute such a defect, either physical or mental or both, to an accident

13. Freud, S.: Die infantile Cerebrallähmung, in Nothnagel, C. W. H.: Specielle Pathologie und Therapie, Vienna, A. Hölder, 1901, vol. 9, pt. 3, p. 180.

14. Collier, James: Brain **47**:1, 1924.

15. Ford, F. R.: Medicine **5**:121, 1926.

of labor, one is removing that stigma. Perhaps this is reason enough to give to one's patients, but the fact remains that many physicians still feel that these defects are due to accidents at birth. This is of some importance, because if physicians arrive at some method by which they can materially reduce or even almost eliminate intracranial hemorrhage of the new-born, they are sure to be disappointed in the results, because they will still have to deal with those conditions which in the past have been erroneously attributed to this accident.

This whole subject is bound up with prognosis. As already stated, a large number of newly born infants die from intracranial hemorrhage. Are physicians in a position to say how many live after that calamity? I fear that in the present state of knowledge they are not. I think that I have shown that in many instances the diagnosis of intracranial hemorrhage of the new-born is impossible, that probably many conditions which have been attributed to this accident are due to other causes and that many of the so-called intracranial hemorrhages of the new-born are nothing more or less than edema or sterile meningitis which clears up in a few days and leaves little if any trace.

Far too much credit has been given to intracranial hemorrhage as a cause of mental and physical defects and far too little to defects of the brain of a developmental nature. Convulsions in the new-born have been attributed far too often to intracranial hemorrhage and much too rarely to edema and to other conditions.

Regarding the treatment, the situation is not so dark, because, happily, preventive measures are of great advantage. The increase in the number of "prenatal clinics," along with the tendency for expectant mothers to consult obstetricians many months before delivery, will certainly result in much better attention at the time of delivery and the prevention of many accidents of birth such as have occurred heretofore. A better knowledge of the physiology of the pregnant mother and her unborn child will result in more strength for the latter and better physical condition for the former. It is to be expected that such professional activities will result in a marked reduction of prematurity, with a consequent reduction in the number of instances of intracranial hemorrhage.

If the hemorrhage has occurred, however, little can be accomplished in the way of treatment. By the time symptoms have presented themselves, the damage to the brain has occurred and is past repair. Relief from tension by lumbar or cisternal puncture has been advocated, but unless the hemorrhage has definitely stopped, such relief from pressure will result in renewed hemorrhage. Operations for decompression are not of value for two reasons: First, the age of the child makes such an extensive operation extremely hazardous, and, second, there is no means of knowing under present conditions where the hemorrhage is. A

possible third reason is that by the time the hemorrhage can be diagnosed the damage to the brain has already taken place. In such an obscure condition there is also the danger that the diagnosis may be wrong and that an unnecessary operative procedure of great severity may be undertaken uselessly.

Doubtless it seems strange that I should have omitted such measures as intramuscular and intravenous transfusions, either of blood or of blood serum and the use of a hypertonic solution of dextrose intravenously. The answer is that I can conceive of no situation associated with intracranial hemorrhage in which either of these measures could possibly be of great benefit. I have therefore not mentioned them.

I am not willing to leave this subject without discussing briefly the future possibilities. The basis of medical care is diagnosis. Without a full knowledge of the condition in hand it is impossible to proceed rationally to its care. Physicians must primarily seek to advance the means of diagnosis in the new-born. They are not at the present time taking full advantage of their opportunities in this respect. The average physician turns his new-born patients over to the care of the nurse and finds it compatible with his dignity to approach them only if something goes wrong. Even then, he is likely to hold up his hands and regard the death of the baby as an act of God rather than as a medical problem. First, this attitude of indifference must be overcome. Then physicians must learn to apply to the new-born the various diagnostic methods which are used on older persons. Not often does one find cultures or chemical studies of the blood made. Infrequently it is thought necessary even to make a blood count or a urinalysis. Roentgenograms of the chest are taken more frequently of late because of the furor aroused by the danger of an enlarged thymus gland. Perhaps this is of advantage if only to show that nothing is known about the thymus gland of the new-born. The increasing knowledge regarding reflex actions and nervous phenomena of the normal new-born infant will eventually aid materially in sensing variations from normal. In the past only an extensive experience could adequately supply this need. It is probable too that physicians may be able to develop diagnostic aids, such as a contrast substance which would give a definite picture of the blood vessels in the brain. Of course, it would take time to interpret the condition in many cases, because there would have to be acquired a knowledge of the normal, but even so this would aid eventually. It is doubtful whether investigation of the spinal fluid obtained by either lumbar or cisternal puncture can be developed further as a diagnostic measure.

Treatment must always rest on early diagnosis. If physicians can arrive at the point at which the diagnosis can be made very early and

the location of the hemorrhage can be placed, then and then only will they be able to arrive at some form of treatment which will be of distinct advantage to the infant.

In summary, intracranial hemorrhage of the new-born is an all too frequent accident of birth and it occurs more frequently after delivery by an inexpert accoucheur than when the physician has been adequately trained. However, in the individual case its prevention must rest on the shoulders of the attending physician, and hard and fast laws must not be laid down, since it is perfectly conceivable, and has doubtless frequently happened, that intracranial hemorrhage of the new-born has resulted from the forces of labor without any interference on the part of the obstetrician and that such interference may have resulted in the prevention of its occurrence in the individual case. This peculiarly serious accident offers difficulties in diagnosis which are insurmountable in many cases at the present time, but it is unquestionably true that in some cases the failure of diagnosis is due to a lack of the employment of facilities which are now offered. That in many cases the condition can and will be prevented by the care of the mother during pregnancy seems without question, but successful treatment of the infant depends on early diagnosis and exact location, and this can be accomplished only by further study of the infant during this period of its existence.

SPECIAL ARTICLES

GRADUATE EDUCATION IN PEDIATRICS

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In 1930 the Committee on Pediatric Education of the third White House Conference on Child Health and Protection passed over the question of graduate education in pediatrics and confined its study to undergraduate instruction in the medical school and to postgraduate instruction by means of short "refresher" courses for practitioners. By graduate education is meant the training of physicians as specialists.

At the meeting of the American Academy of Pediatrics in Atlantic City in 1931 the Committee on Medical Education was directed to study and report on pediatrics as a restricted field of practice. This study was undertaken and was continued for two years. The first report was based on approximately 300 opinions gathered from the members of the academy as to the minimum and the ideal training and education necessary for specialists in pediatrics.[1] Such a study was necessary because no factual data were available.

The majority of the members seemed to feel that three years of training after graduation was necessary, including one year of internship in a general hospital and two years of study restricted to pediatrics. Ideal training was thought by 50 per cent to require four years of study. Those urging a three year period expressed fear of "overhospitalization."

The committee finally outlined an ideal training as follows:

1. Graduation from a class A medical school.

2. One year of general hospital training.

3. Two years of service in a hospital for children, the service to include clinical work in the wards, work in the outpatient department, the well baby clinic and the contagious disease service and training in preventive pediatrics and child guidance (mental hygiene).

4. One year of special work in pediatrics, to fill in gaps in the service outlined and to include investigation, further clinical study and/or study in Europe.

Prepared for and approved by the American Board of Pediatrics.

1. Proceedings of the First and Second Annual Meetings of the American Academy of Pediatrics, J. Pediat. **1**:519, 1932.

With few exceptions not more than two years of the last three should be spent in the same institution.

The committee made no attempt to fix standards but merely tried to obtain and express an average of the opinions of a large number of practicing pediatricians.

Continuing its work, this committee, after a two year study of pediatrics as a restricted field of practice, recommended at the Chicago meeting of the academy in 1933 the formation of a certifying board, the American Board of Pediatrics.[2] Its suggestion was approved by the academy, by the American Pediatric Society and by the Section on Pediatrics of the American Medical Association, and three members were appointed by each organization to constitute the board.

The question of specialization was thus transferred from the committee of the academy to the American Board of Pediatrics by action of the academy. Two of the eight members of the academy committee were among the nine members appointed to the board. The fact that the chairman of the academy committee was made president of the board tended to confuse the work of the two bodies and may have resulted in some misunderstanding.

The American Board of Pediatrics in a recent report [3] portrayed the development of specialty qualifying boards and their relationship to the American Medical Association through its Council on Medical Education. It is to be hoped that the certification of specialists by boards, which are active or soon to be active in eleven fields of specialized practice, will become firmly entrenched in American medical institutions and will bring order out of chaos. Naturally, with this development many problems and questions in connection with graduate education in pediatrics have arisen.

The Board of Pediatrics has taken the attitude that its specific function is the certification of men who apply to it after having completed a certain minimum period of training. At present this period is similar for all specialties. It was determined on after numerous conferences and is not to be changed at will by any individual board. It closely approximates the ideal training previously outlined. The details as to what must be included are matters for the consideration of the individual boards.

The control of education by the boards is limited to the examinations. The pediatric board feels that it is not its function to attempt

2. Report of the Committee on Medical Education for 1933, Proceedings of the American Academy of Pediatrics, J. Pediat. **2**:501, 1933.

3. Veeder, Borden S., and Aldrich, C. A.: Report of the American Board of Pediatrics, Inc., Am. J. Dis. Child. **51**:389 (Feb.) 1936.

in any way to make rules and regulations about the details of the training of residents in hospitals. It does not believe in fixed or regimented methods imposed by any outside authority. It does, however, have convictions about what the applicant should know, and it feels that persons not adequately taught will fail in the examinations. As time goes on, young physicians who intend to enter pediatrics will naturally select the institutions which have graduated successful candidates.

On the other hand, the board is desirous of helping by pointing out in a general way what deficiencies in the training of candidates are revealed by the examinations. It has already called attention to the fact that the largest number of failures have taken place in examinations on the subject of growth and development.

Today 95 per cent or more of the men who are planning to specialize in pediatrics obtained their graduate education through serving as residents in hospitals for children. The "approved list" of the Council on Medical Education of the American Medical Association, which is used, lists 283 such positions in 81 hospitals. Of these hospitals, 52, with 69 per cent of the residencies, are connected with medical schools where undergraduate instruction is carried on. Twenty-nine hospitals have no such connections, and these furnish 88, or 31 per cent, of the approved residencies. In addition, 20 of the approved hospitals offer internships (81 all told) in pediatrics, which, under the rules adopted by all the specialty qualifying boards, do not count as part of specialized graduate education. The training given the Fellows of the Mayo Foundation is most satisfactory. It does not seem probable, however, that a similar type of graduate education will be adopted by other institutions. Only one school, the University of Pennsylvania, offers a graduate course of instruction, and it seems unlikely that a similar course will be offered by other educational institutions. For practical purposes, therefore, a discussion of graduate education in pediatrics limits itself almost wholly to hospital residencies.

Obviously there are marked differences in the quality of the training afforded by these residencies. In some it seems inadequate. The board feels that a detailed survey of hospital services should be made, but it does not feel that this is the duty of the board. The board has a direct relation with the candidate as an individual, but not with the institution which he selected for his training. It feels that such a survey is a proper activity for the American Academy of Pediatrics, as it is a stated purpose of the academy to elevate standards in the field of pediatrics. The academy committee recommended in its report

this year [4] that the executive committee attempt to obtain funds for this type of study. While the board has called attention to the importance of such a survey, it feels that it should be independently carried out. A survey of residencies in all fields, similar to the recent survey of medical schools, has been discussed by the Advisory Board for Medical Specialties.

In compliance with an action of the Advisory Board for Medical Specialties, applying to all boards, and in response to many requests, including one from the American Hospital Association, the American Board of Pediatrics has prepared a statement of what it feels pediatric hospital training should include (see appendix). It is not an attempt to dictate in any way to the various hospital services, but is intended to suggest what experience has shown should be included in satisfactory training for the pediatrician. It makes no attempt to state such factors as time, order or arrangement of the subjects, as these are not within its province. It does not say that an approved residency must offer all these services but simply points out the ground that should be covered by the young physician who is obtaining his graduate training in a residency.

BASIC TRAINING

A second matter for discussion arose from a ruling of the Advisory Board for Medical Specialties and the Council on Medical Education of the American Medical Association. It should be remembered that no specialty qualifying board may be admitted to the advisory board unless its rules meet the standards prescribed by them and that no individual board or its licentiates will be recognized by the council of the American Medical Association unless it is recognized by the advisory board.

This point, which has been a problem to the pediatric board, and in turn has become one to the 81 hospitals where graduate education is carried on, relates to a clause which states that effective Jan. 1, 1938, special training must include: "intensive graduate training in anatomy, physiology, pathology and the other basic medical sciences which are necessary to the proper understanding of the specialty in question."

There is not and cannot be any attempt on the part of the council or of the advisory board to define basic training except in these general terms. A specific definition is the function of the various boards. The trouble arises from the fact that the pediatric board itself has been puzzled as to just what it should suggest as basic training in the sciences underlying pediatrics.

4. Report of the Committee on Medical Education, Proceedings of the Sixth Annual Meeting of the American Academy of Pediatrics, J. Pediat. **7**:786, 1936.

During the past year, by personal discussion or by correspondence, nearly one hundred pediatricians were sounded in an attempt to obtain the ideas and thoughts of the men who were (1) directors of the hospital services which furnish graduate education and (2) active practitioners in touch with the needs of persons who are entering pediatric practice. It is impossible to give in detail all the ideas mentioned, but certain thoughts have been so consistently expressed that a picture of what is basic training in pediatrics is slowly taking definite shape.

It should be kept in mind that we are discussing basic training for the pediatrician who will enter practice and not for the one who will enter an academic life. The latter may well spend one or more years in one of the basic medical sciences.

Almost without exception the first point raised referred to the peculiar character of pediatrics as compared with other restricted fields of practice. Pediatrics includes all the fields of medicine and is in reality general practice limited to an age period. All basic medical sciences, therefore, underlie pediatrics and are necessary to its understanding. To make, however, as has been suggested, each graduate student devote a certain definite time, such as three or six months, in a basic department, such as anatomy, physiology, biochemistry or pathology, would not help his special training except in that particular line. To require training in all basic fields would reduce the problem to an absurdity. The time element alone would make the requirement impossible, to say nothing of the practical impossibility of finding the necessary places in the basic departments. The newly formed Board for Internal Medicine will find itself confronting the same situation. Much of the opinion expressed was against required periods of study in any basic field. Perhaps the problem can be summed up, as one pediatrician expressed it, by saying that the entire medical school course forms the basic training in pediatrics.

In many discussions the importance of pathology, immunology, chemistry, etc., was stressed. Nearly every pediatrician has come to the conclusion that such subjects can be made integral parts of routine graduate medical training in the hospital so far as they apply specifically to pediatrics, and in part they are being so made. If every hospital had a clinical pathologic conference weekly or biweekly, with required attendance of the house staff, the clinical chief and the pathologist, the needs of pathology would be amply filled in two years of residency. If each resident was required not only to do the mechanical work of drawing blood from a vein but in addition to do the plating and identification of a certain number of blood cultures, etc., under supervision of the pathologist, the basic needs of bacteriology as applied to

pediatrics could be covered. In a similar manner, the princples and technics for the basic sciences as applied to pediatrics could be reviewed and covered. In many hospitals this is now being done. In other words, it would be a relatively simple matter in the routine training of the resident in the hospital to refresh him, so to speak, as to technical procedures. The study of certain phases, such as public health measures, which are closely related to pediatrics, could be arranged.

In certain specialties, basic training courses are given during the period of residency. For example, in ophthalmology forty hours of anatomy of the eye, forty hours of physiology of the eye, forty hours of pathology of the eye, etc., are given. This is easily done in a specialty which is limited to one anatomic part or system of the body.

We must return, as has been said so often, to the fact that pediatrics centers on the child. Basic training logically centers on a knowledge and understanding of the child. The thing that differentiates the child from the adult is the fact that the child is a growing, developing organism. It logically follows that a knowledge of growth and development is the distinguishing requirement for an understanding of the specialty.

Anatomy, biochemistry, physiology, biometrics and psychology form parts of this subject. We can think of no other solution to the problem of basic training than that some form of definite didactic course associated with practical exercises be attempted during the residencies. How the course should be given and of what it should consist is unclear. Hospitals connected with medical schools, in fulfilling the requirements for basic training, should have little difficulty in finding capable and competent staffs to provide such a course. This probably does not hold true for hospitals now approved which do not have university connections. Two plans have been suggested to meet the situation. One is that an intensive short course be given once a year in three or four medical centers. The second is that a correspondence course be provided. The latter method is now being studied by four members of the board.

The time has arrived when something definite must be started to provide basic training in the subject of the growth and development of the child. A group or committee can do no more than point out the general content of the necessary course. How, when and where it is to be given is the problem of the hospitals which offer graduate education in pediatrics. The project will require several years of experimentation and change before ideal attainment is possible. Several hospitals have already taken the first steps by a series of special lectures or conferences with the resident staff, but no hospital has as yet entered on what might be called a complete program.

The statement has been made that the instruction might interfere with the routine work of the resident staff. Few will disagree, however, with the premise that the hospital has a definite obligation to its house staff. If it seeks house officers directly, or even indirectly by offering to the recent graduate the opportunity to obtain a specialized training in pediatrics, it seems but honest and fair that it should give him the education which will enable him to practice his specialty intelligently. We feel that this cannot be done without adequate instruction in growth and development.

At present any statement as to the time required for a satisfactory course including the essentials from the standpoint of anatomy, chemistry, biometrics and psychology would be a matter of individual opinion. The course would require a fair-sized staff and considerable experimentation as to the proper balance and adjustment of time. From discussions, an opinion might be hazarded that a course of eighty hours, two hours a week for forty weeks, would cover the requirements so far as time is concerned, although there are no factual data available to support this opinion. This course, combined with more definite review work in pathology, bacteriology, etc., as a part of the routine work of the resident, would adequately cover training in the basic medical sciences underlying pediatrics as a specialty, in the opinion of the great majority of practicing pediatricians and teachers of pediatrics in the medical schools. The American Board of Pediatrics is in agreement with this opinion.

APPENDIX: SCOPE OF GRADUATE EDUCATION IN PEDIATRICS

At present many hospitals with pediatric residencies lack one or more services essential to the training of the pediatrician, and many applications are being filed at hospitals where the education may be regarded as incomplete, although the time requisites have been fulfilled.

After considerable discussion the American Board of Pediatrics has drawn up the following outline of what it considers essential in the education of the pediatrician so far as scope is concerned. It realizes that every hospital cannot offer all these services, and hence the outline is to be considered not as a set of rules or regulations adopted by the board but rather as a memorandum of suggestions for a goal to be aimed at by the hospitals and of advice to the recent graduate who is entering on the study of pediatrics as a specialty. When important services, such as that for the new-born or for contagious diseases, are not available to the graduate student, the resultant gaps in his training should be made up during the two following years of "continued study and practice" as outlined in the regulations of the board.

The essential services and educational divisions may be discussed under seven headings:

1. Clinical service in infant and general medical wards, including laboratory study in the assigned cases.
2. Outpatient service.
3. Contagious disease service.
4. Service for the newly-born in connection with the maternity department.
5. Well baby or infant welfare service.
6. Mental hygiene in childhood.
7. Growth and development.

1. *Clinical Ward Service.*—Most of the two years of residency is and should be spent in clinical work in the wards. This should provide the necessary training in pediatric diagnosis and in diagnostic procedures, such as examination of the blood and the urine, interpretation of roentgenograms and lumbar puncture, as well as in treatment and therapeutic procedures, such as transfusion and hydrotherapy. The value of clinical work in the wards to the resident depends not so much on the number of patients observed as on the care and detail with which they are studied and the attitude and interest of the members of the hospital staff.

Opportunity to study the pathology of childhood during the residency should be provided by clinical pathologic conferences at stated times.

In addition to routine laboratory examinations, the resident should be required to carry out a limited number of technical procedures, such as cultures and chemical examinations of the blood, and spinal and cisternal punctures, reviewing the work of the basic sciences taught in the first two years of medical school. These should be in connection with his clinical cases.

2. *Outpatient Service.*—Service and training in the outpatient department are essential, as it is there that the material resembles most closely that seen in practice. Many hospitals offer outpatient service as a part of the second year of residency. Assignment to the hospital admitting room, where patients apply for examination, admission or emergency treatment, offers a partial and incomplete substitute, as the patients are not followed.

3. *Contagious Disease Service.*—Only a limited number of residencies offer this service. Some hospitals have arrangements whereby the junior residents serve in turn for a limited period in a hospital for infectious disease. A number of short term (from two to six months) services are available in hospitals for infectious disease, which may be taken after the two years of pediatric residency are over.

4. *Service for the New-Born.*—Experience with the new-born is essential for the pediatrician. In an increasing number of maternity departments the care of the new-born is assigned to a pediatric service and hence is available to the pediatric resident. Service with the new-born should be obtained subsequently when it is not available during the period of residency.

5. *Infant Welfare Service.*—As a large part of the work of the pediatrician has to do with the care of the well baby, it is essential that graduate training include service in a well baby clinic or infant welfare station, where the growth and development and the feeding of well infants, as contrasted with the care of sick

infants in the hospital wards, can be followed. The service should not be crowded into a few weeks but should be so arranged as to permit the following of a small group of infants over a number of months.

6. *Child Guidance, or Mental Hygiene.*—At present this subject presents a difficult problem, as only a few hospitals for children have integral or associated psychiatric departments. During the past three years there has been an increasing tendency to form such departments, and seemingly it will be possible within a few years to offer training in the psychiatric approach to residents in children's hospitals. As a general rule the child guidance clinics not associated with medical institutions have made no provision for a brief, limited training for graduate students in pediatrics.

7. *Growth and Development.*—Education in this field is necessary to basic training for pediatrics. The board, after careful study and consideration, recommends the development of a regular didactic course to be given to the resident staff to cover the subject. Such a course is discussed more fully in the first part of this report.

The American Board of Pediatrics feels that adequate graduate education in pediatrics should include training in all the fields and services in the preceding outline. When the hospital residency fails to provide this, the graduate student should make up deficiencies during the two years of "continued study and practice" which are a part of the requirement for appearance before the board for examination. A hospital residency of two years which fails to cover these subjects cannot be regarded by the graduate student as satisfactory, even if it is on the "approved list" of pediatric residencies.

News and Comment

UNIVERSITY NEWS

From September 30 to October 13 the University of Vienna will give its usual course for physicians. It will include, as is customary, excellent clinics on children's diseases conducted by Dr. Franz Hamburger.

Three years ago the Mississippi State Medical Association, through its House of Delegates, decided to give postgraduate extension programs. In 1934 a course in obstetrics was inaugurated. Questionnaires were then sent out, and approximately 90 per cent of the replies asked for instruction in pediatrics. This year lectures are to be given throughout the state by Dr. Robert A. Strong, professor of pediatrics at the Tulane University of Louisiana School of Medicine.

DEATHS

Dr. Robert K. Rewalt of Williamsport, Pa., a well known pediatrician of that state, died suddenly on July 27.

Abstracts from Current Literature

Biochemistry, Bacteriology and Pathology

STUDIES ON THE SOLUBILITY OF PNEUMOCOCCUS IN SAPONIN. SIDNEY J. KLEIN, J. Bact. **30**:43 (July) 1935.

Klein considers saponin a useful reagent in differentiating between pneumococci and streptococci. The saponin test was found just as expedient and reliable as the bile test. The separation of these two bacterial species is of such great practical and theoretical significance that any additional differential test may prove of importance. According to the author, the following characteristics of the saponin lysis reaction deserve emphasis:

1. The simplicity of the "sensitization" technic.

2. The rapidity of the lysis reaction. The time required for lysis varies with the concentrations of the sensitizing substance and of the saponin. With saponin in concentration of 1:20 and cholesterol in concentration of from 1:5,000 to 1:500,000, lysis often appears within a few minutes and is usually complete within thirty minutes at room temperature. The bacterial suspension becomes completely clarified and transparent. No intact bacteria are to be observed on microscopic examination in the case of complete lysis.

3. The high degree of bacteriolytic power possessed by saponin. Lysis is somewhat slower with the saponin in a 1:1,000 dilution; however even a 1:20,000 dilution shows strong bacteriolytic activity for "sensitized" pneumococci.

4. The ready solubility of saponin in water and the stability of the sterile aqueous solution. The saponin solution may be sterilized by autoclaving without apparent diminution of its bacteriolytic activity, whereupon it will keep for a long time.

5. The availability and inexpensiveness of the reagents.

STOESSER, Minneapolis.

THE SILICON DIOXIDE CONTENT OF THE LUNGS OF INFANTS AND OF PLACENTAL TISSUE. WILLIAM D. MCNALLY and W. L. BERGMAN, J. Indust. Hyg. **17**:171, 1935.

Silicon dioxide is a normal constituent of all tissues of the human body. It is present in the fetal lung, in the placenta, in the umbilical cord and in the placental blood. The presence of fluorides in the blood accounts for the formation of fibrous tissue from inhaled silica and strengthens the opinion previously rendered that silicosis is caused by chemical rather than by traumatic action.

FROM THE AUTHORS' SUMMARY. [ARCH. PATH.]

A SIMPLE METHOD FOR THE ADMINISTRATION OF THE ESTROGENIC SUBSTANCES OF URINE. ARTHUR GROLLMAN, HARRIS B. SHUMACKER JR. and EVELYN HOWARD, J. Pharmacol. & Exper. Therap. **54**:393 (Aug.) 1935.

The authors found that estrogenic substances can be readily extracted from urine by adsorption on charcoal. When the adsorbed substance is given by mouth to laboratory animals estrogenic phenomena result. While anterior pituitary-like substances can be adsorbed by charcoal, the product is inactive when given by mouth, and it has been shown by others that anterior pituitary-like substances are destroyed in the gastro-intestinal tract.

PILCHER, Cleveland.

CYTOLOGICAL EXAMINATION OF MILK FOR TUBERCLE BACILLI. S. T. COWAN and L. MADDOCKS, J. Path. & Bact. **41**:373, 1935.

A method of making films for a cytologic examination of milk is described. Several varieties of cellular aggregation are seen in tuberculous and nontuberculous milk, but of these only three types of endothelioid cell groups appear to be of importance. The presence of endothelioid cell groups in a sample of milk is not evidence of tuberculous infection, but it is thought to be indicative of some form of mastitis. The examination of endothelioid cell groups facilitates the demonstration of acid-fast bacilli in films of milk, and in a series of 229 samples of unmixed milk 21 of 38 tuberculous samples (55.3 per cent) were detected by this means. The demonstration of acid-fast bacilli in an endothelioid cell group is considered to have much greater diagnostic significance than their demonstration without relation to the cytology of the film. No false positive results were obtained in this series, and in our opinion a report can be issued with confidence that Mycobacterium tuberculosis was present.

FROM THE AUTHORS' SUMMARY. [ARCH. PATH.]

Metabolism; Infant Feeding; Milk and Other Foods

THE EFFECT OF DIET ON THE HEMOGLOBIN CONCENTRATION OF THE BLOOD. L. N. ELLIS and O. A. BESSEY, Am. J. Physiol. **113**:582 (Nov.) 1935.

Determinations of the hemoglobin were made on rats at 1 month and 1 year of age to study the influence of five diets. At 1 month of age the hemoglobin concentration increased along with the iron content of the ration. The adult rats showed only small differences and not the same relationship to the iron content of the diets.

NOURSE, Cleveland.

MILK. LOUIS FISCHER, Arch. Pediat. **52**:781 (Nov.) 1935.

Not abstracted.

WADDELL JR., University, Va.

EFFECTS OF INCREASING THE CALCIUM CONTENT OF A DIET IN WHICH CALCIUM IS ONE OF THE LIMITING FACTORS. H. C. SHERMAN and H. L. CAMPBELL, J. Nutrition **10**:363 (Oct.) 1935.

In previous work Sherman and Campbell have shown that a diet adequate to maintain normal growth, health, reproduction and lactation for generations may be further improved so that better nutritional well-being results.

Because it was felt that there are certain limiting factors which determine this improvement and that calcium might be one of these factors, experiments were conducted on rats. One group was placed on the known adequate diet and another group on the same diet, to which calcium carbonate was added. The calcium content of the mixture of dry food was increased from 0.2 to 0.35 per cent in the second diet.

The results indicate that the increased intake of calcium was partly responsible among the rats for the better growth, earlier maturity, longer period between the attainment of maturity and the onset of senility; and, in less degree, an increase in the life expectation of the adults which were observed. The mortality for the young was also decreased. In general, the results of the experiment indicate that the level of the intake of calcium most conducive to optimal well-being is significantly higher than that required for normal growth and maintenance.

MUNNS, Winnetka, Ill.

FOOD PROBLEMS IN THE ONE CHILD FAMILY. MAX R. WOODWARD, South. M. J. **28**:946 (Oct.) 1935.

Woodward believes that mothers should be taught to feed a child as though he had six hungry brothers and sisters and to treat him with judicious neglect

that food must not be discussed in the child's presence, that there are no authentic cases on record in which normal children have starved to death in the presence of food, that all children do not take or require the same amount of food and that the mother's duty ends with the provision of attractive, wholesome food served at proper intervals.

SCHLUTZ, Chicago.

SOME ASPECTS OF INFANT FEEDING. H. BOYD GRAHAM, Brit. M. J. **2**:614 (Oct. 5) 1935.

This article outlines Graham's ideas on the feeding of infants on the basis of his own experience and that of others.

ROYSTER, University, Va.

STUDIES OF ACIDOSIS BY ASPHYXIA. D. CORDIER, Ann. de physiol. **11**:138, 1935.

Studies were made on a dog whose vagus nerve was cut which was subjected to progressively increasing asphyxia due to lack of oxygen.

The ventilation of the dog increases as the oxygen diminishes in the inspired air. The animal dies when the oxygen in the inspired air falls to 2.5 or 3 per cent. The total carbonic acid content of the arterial plasma diminishes from the beginning of the asphyxia and falls as low as 10 volumes per cent when the animal dies.

In asphyxia due to lack of oxygen both the normal dog and the dog whose vagus is cut show hyperventilation and acidosis. Vagotomy does not seem to diminish the resistance of the dog to asphyxia.

These results are contrary to those of Haggard and Henderson and confirm the existence of acidosis due to asphyxia.

BUDSON, Detroit.

ACETONURIA AND ACIDOSIS IN INFANCY. EUGENIO CIENFUEGOS, Arch. de pediat., Rio de Janeiro **7**:129 (Dec.) 1935.

Acidosis and acetonuria are terms that should be distinguished. Acetonuria means the elimination of acetone bodies in the urine and is a frequent symptom. It is a sign of abnormal metabolism. Acidosis, on the other hand, is a toxic symptom due to renal or hepatic insufficiency caused by the faulty metabolism of fats or carbohydrates. It can be determined by estimation of the carbon dioxide combining power of the blood plasma.

SANFORD, Chicago.

MIXED FEEDING. LUIS MORQUIO, Bol. Inst. internac. am. de protec. a la infancia **9**:230 (Oct.) 1935.

Morquio states that breast milk is the food that best insures the health of the child and that every healthy mother is totally or partially capable of feeding her child.

Mixed feeding is a powerful resource when, through diverse circumstances, the child is inadequately fed, but on the condition that the complementary food does not impair breast feeding; to this end the mother should be properly guided by the physician or his auxiliaries.

All public and private organizations for the welfare of infants should keep in sight the fact that unless mixed feeding is properly directed it leads to the substitution of breast feeding. This represents a dangerous situation that should be avoided if the end of such organizations is not to be misunderstood.

LESLIE, Evanston, Ill.

EFFECT OF GLYCERIN ON BLOOD SUGAR. HANS O. BEHRENS, Monatschr. f. Kinderh. **63**:368, 1935.

There has been some difference of opinion as to the effect of fat on the amount of blood sugar. Behrens investigated the problem further by determining the effect

of glycerin on the sugar content of the blood. In five children he was unable to elicit any effect following the administration of 30 Gm. of glycerin in 150 cc. of water.

GERSTLEY, Chicago.

A NEW MILK REACTION. ALPHONS SOLÉ, Monatschr. f. Kinderh. **63**:383, 1935.

By using a hematoxylin preparation, Solé is able to differentiate by means of the resulting color reactions: (1) breast milk from uncooked cow's or goat's milk, (2) breast milk from boiled breast milk, (3) cow's milk or goat's milk from boiled cow's milk or goat's milk, (4) the souring of milk and (5) the nature of pasteurization of cow's milk.

GERSTLEY, Chicago.

CREATINE AND CREATININE METABOLISM. HANS KLEINSCHMIDT, Monatschr. f. Kinderh. **64**:1, 1935.

Five of seven healthy children showed disappearance of creatine from the urine when placed on a diet without animal protein. This phenomenon has seldom been noted. Large doses of amino-acetic acid led to an increased excretion of creatine in six children. Formerly this was considered pathognomonic of a myopathy. When the healthy children were fed large doses of creatine they showed better retention than children with diseased muscles.

In children sick with a myopathy large amounts of creatine are excreted, even when the diet is free from creatine. In the sick group the feeding of amino-acetic acid caused a definite increase in creatinuria. This is not necessarily greater than in the healthy group. The reactions are greatest in the Erb type of dystrophy. In the diseased group the feeding of creatine gave indefinite results. The retention was highest in the Erb dystrophy.

Th excretion of creatinine is highest in the children with normal muscles. There is an indefinite parallelism between the degree of diminution of the excretion and the severity of the disease in the myopathies.

Treatment with amino-acetic acid was unsuccessful in the cases of progressive muscular dystrophy.

GERSTLEY, Chicago.

INVESTIGATIONS ON HYPERLIPEMIA AND CHOLESTEROLURIA. JENS BING and U. STARUP, Acta med. Scandinav. **86**:12, 1935.

In patients with nephrosis the high cholesterol content of the blood is not due to the low content of the serum protein or to the anemia. The excretion of cholesterol changes parallel to the glomerular filtration, independently of the diuresis, though no correlation was found between the cholesterol content of the blood and the excretion of cholesterol. Proteins show a similar behavior.

KAJDI, Baltimore.

Vitamins; Avitaminoses

HEMOLYTIC ACTION OF CEVITAMIC (ASCORBIC) ACID. H. H. ANDERSON and C. D. LEAKE, J. A. M. A. **105**:1033 (Sept. 28) 1935.

Concentrations of 1:1,000 or stronger of natural or synthetic cevitamic acid in physiologic solution of sodium chloride or water cause immediate hemolysis. No hemolysis occurs within forty-eight hours in dilutions of 1:5,000 or weaker in 0.9 per cent solution of sodium chloride. A patient given 100 mg. of the acid dissolved in 10 cc. of sterile distilled water by vein showed a reaction which was thought to be due to the hemolytic effect of the acid. It is, therefore, suggested that for intravenous use solutions of the sodium salt of cevitamic acid approximate isotonicity, i. e., 1 per cent of the salt dissolved in physiologic solution of sodium

chloride or 3 per cent of the salt dissolved in distilled water. If only the acid is available it should be neutralized with half its weight of sodium bicarbonate in physiologic solution of sodium chloride before injection.

BONAR, Salt Lake City.

RELATIONSHIP BETWEEN INFECTION AND THE OCULAR TERRAIN IN AVITAMINOSIS. A. G. MORIQUAND, Paris méd. **2**:23 (July 6) 1935.

It is claimed that lack of vitamin A produces changes in the ocular tissues which make them particularly vulnerable to infection.

LESLIE, Evanston, Ill.

BERIBERI, A DISEASE OF ALIMENTARY DISEQUILIBRIUM. R. LECOQ, Progrès méd., Aug. 24, 1935, p. 1381.

The author, from his experiments on pigeons and observations on the European and the native of Indo-China, concludes that beriberi is fundamentally due to an alimentary disequilibrium in which there is an overproduction of fatty acids from glucides. This may depend on the diet alone or on the action of certain organisms inhabiting the alimentary tract, particularly Bacillus asthenogenes. It may be produced by castor oil, the peptone of egg albumin or lactose.

LESLIE, Evanston, Ill.

RICKETS: ITS PATHOGENESIS. A. B. MARFAN, Rev. franç. de puériculture **2**:257 (Nov.) 1934.

The bony lesions of rickets result from the reactions of the cells in the zone of ossification to intense or prolonged infections and intoxications which occur at the period of growth of the bone, especially during the last month of fetal life and the first months of extra-uterine life. At first it is the medullary cells which show the greatest reaction, but soon the cartilage cells and osteoblasts participate.

The infections and intoxications seem unable to produce rickets except in the absence of a special principle which protects the cells of the zone of ossification. This antirachitic principle, or vitamin D, has been identified as viosterol. Impoverishment of the organism of this principle permits infections and intoxications to produce the bony reactions. This impoverishment may be due either to the lack of the action of sunlight on the organism or to the infectious or toxic malady itself, which diminishes the production or favors the destruction of the antirachitic principle.

CRANE, Chicago.

VITAMIN B DEFICIENCY IN CUBA; THE PELLAGROID SYNDROME BERIBERI. AUGUSTIN CASTELLANOS, Bol. Soc. cubana de pediat. **7**:5 (Jan.) 1935.

Castellanos is of the opinion that vitamin B deficiency is not uncommon among Cuban children, particularly among the poorer classes of peasants and workmen. The food available to them is often inadequate and almost always of poor quality. Negro and mulatto children between the ages of 8 months and 4 years are generally affected. Their diet is usually deficient in milk and vegetables.

Wasting, with edema in the extremities, is one of the earliest symptoms. This is followed by erythema involving the edematous portions of the extremities, which may also occur on the face and which may resemble the exanthem of rubeola. On the distal parts of the extremities—the hands and feet and the lower third of the forearms and the legs—the erythema is uniform, as in scarlet fever. The color changes from red to brown when desquamation begins and finally leaves the underlying areas of skin dry and shriveled. Nervous and motor symptoms then set in. The affected extremities show hypesthesia.

The patients often show stupor and great apathy. All the symptoms are progressive unless the condition is relieved. There is seldom any fever, and there is practically no digestive disturbance. Rickets and xeroderma often complicate the disorder.

Complete recovery is possible if the proper dietary regimen is instituted. The disorder may easily be mistaken for acrodynia. SCHLUTZ, Chicago.

SUBPERIOSTEAL HEMORRHAGES OF SCORBUTIC ORIGIN. M. TORELLÓ CENDRA, But. Soc. catalana de pediat. **6**:97 (March-April) 1933.

A case of scurvy is reported in a nursling 8 months old. The author describes a new roentgenologic sign, namely, a protruding spine (espina diafisaria) at the end of the bone, usually found at the lower end of the femur or the upper or the lower end of the tibia. WATSON, Elmhurst, Ill.

REVISION OF THE ROENTGENOGRAPHIC SYMPTOMS OF SCURVY. J. ESTEBAN FERRER, But. Soc. catalana de pediat. **6**:108 (March-April) 1933.

Emphasis is placed on the important contribution of roentgen ray examination in the diagnosis of scurvy. WATSON, Elmhurst, Ill.

A CASE OF SCURVY. ODILON DE ANDRADE FILHO, J. de pediat., Rio de Janeiro **2**:285 (July) 1935.

The author reports a case of scurvy in a child 11 months old. Roentgenograms are shown. A complete description of the physiologic symptoms, as well as of the prescurvy stage, is given. Of interest is the blood calcium content, which was 8.4 mg. per hundred cubic centimeters. The use and action of cevitamic acid (introduced as ascorbic acid) are discussed. SANFORD, Chicago.

PLASMA PHOSPHATASE VALUES OF NORMAL AND RACHITIC CHILDREN. OLUF ANDERSEN, Jahrb. f. Kinderh. **44**:206 (April) 1935.

The literature and history concerning phosphatase are reviewed. Phosphatase is defined as an enzyme that has the capacity to split off inorganic phosphorus from organic phosphorus compounds.

From determinations of the phosphatase values for oxalated plasma, made on thirteen nonrachitic children up to 3 years of age, on twelve nonrachitic children from 3 to 13 years of age and on twenty-one rachitic children from 3 to 27 months of age, the following conclusions were reached:

Phosphatase values under 30 units are not elevated. Phosphatase values between 30 and 40 units are suspiciously elevated. Phosphatase values above 40 units are definitely elevated.

Antirachitic therapy causes a diminution of the phosphatase values in rachitic children. This value declines while the values for phosphorus and calcium are climbing. The decline in the phosphatase values takes place much more slowly than the rise in the other values and seems to give a truer picture of the clinical improvement. The finding of an elevated level of blood phosphatase without clinical signs of rickets can be taken to mean latent avitaminosis D.

LANDAU, Rochester, N. Y.

VITAMIN C AND THE BLOOD. A. BÖGER and W. MARTIN, München. med. Wchnschr. **82**:899 (June 7) 1935.

The authors studied the effects of vitamin C (cevitamic acid) therapy in various diseases. They concluded that vitamin C affects the blood and the blood-forming

tissues in four ways: It (1) decreases the permeability of the blood vessels, (2) increases the number of platelets by action on the bone marrow, (3) increases the serum albumin by action on the plasma proteins and (4) improves the coagulation of the blood.

BRAHDY, Mount Vernon, N. Y.

VITAMIN CONTENT OF VARIOUS DIETS. H. SCHROEDER and V. WITTMAN, München. med. Wchnschr. **82**:988 (June 21) 1935.

It has been maintained that there is no danger of avitaminosis if a person eats a well balanced diet. Since the isolation and synthesis of various vitamins it has been possible to prevent and treat the avitaminoses, as well as to determine the vitamin content of foods. An intermediate stage in some vitamin deficiencies—hypovitaminosis—has been recognized.

Although the diet may be normal, hypovitaminosis may occur. The vitamin requirement is greater for the growing child than for the adult. Patients with infections, diabetes or carcinoma have an increased vitamin requirement. The absorption of vitamin may be diminished or the vitamin may be destroyed in the intestine during certain gastro-enteritides. In addition, an excess of carbohydrate or alcohol in the diet may increase the requirement for vitamin B_1. The interdependence of calcium, phosphorus and vitamin D in the development of rickets is well known.

According to Stepp, the vitamin requirements for man are as follows:

Vitamin A: minimum, 1 mg. of carotene; optimum, from 3 to 5 mg. (not definitely known).

Vitamin B_1: minimum, from 0.75 to 1 mg. of the crystalline form of vitamin B_1 (Windaus).

Vitamin B_2: minimum, 1 mg. of lactoflavine; optimum, from 3 to 5 mg.

Vitamin C: minimum, for infants, 2.5 mg. of the crystalline form of cevitamic acid (introduced as ascorbic acid); for adults, from 10 to 20 mg.

Vitamin D: for infants and children, minimum, 0.002 mg. of the crystalline form of vitamin D_2 (calciferol); optimum (which is also the minimum for rickets), 0.01 mg. The amount for adults is not known, but is not much greater.

Vitamin E: The requirement is not known.

Schroeder and Wittman tabulated the vitamin content of various diets which patients receive. In most of the diets the content of vitamin A and that of vitamin D were adequate. A deficiency of vitamin C was more frequent. Only a few diets contained the minimum requirement of vitamin B_1, but vitamin B_2 was more adequately supplied.

BRAHDY, Mount Vernon, N. Y.

KERATINIZATION OF THE EPITHELIUM OF THE MUCOUS MEMBRANES CAUSED BY LACK OF VITAMIN A AND CAROTENE: THE ANTI-INFECTION ACTION OF VITAMIN A. HANS VON EULER and M. MALMBERG, Ztschr. f. physiol. Chem. **232**:1, 1935.

The authors were unable to demonstrate any evidence of prolapse of the vagina or xerophthalmia in fifteen white mice when on a diet free from vitamin A. In 1931-1932 there occurred an epidemic of infections due to hemolytic bacteria in their animal colony. Of the seven hundred rats which they had under observation, only those which had been without carotene or vitamin A during their developmental period were stricken with the disease. The animals which were used for the study of the effects of vitamin D and which had had carotene in the diet were free from the infection. Studies of the antibody formation in these animals were made by other workers. Von Euler and Schmidt previously had found that the purine content of the young tissues was increased when the animals were on a diet rich in vitamin A and carotene. This suggested that the anti-infectious effect

of vitamin A lies in the increase in the purine, which allows for the building of the cell nucleus. This suggests further study of cell histology in the question of the anti-infectious feature of vitamin A.

HANSEN, Minneapolis.

ACIDOSIS IN INFANTILE BERIBERI. I. KOBAYASHI, J. Pediat. (Tokyo), no. 422, July 20, 1935, p. 909.

The average carbon dioxide combining power of the blood of normal children was found to be 46 volumes per cent (maximum, 55; minimum, 42), while the blood of patients with infantile beriberi showed an average of 41 volumes per cent (maximum, 54; minimum, 28). The degree of acidosis is most severe in the cardiac type of the disease.

KATO, Chicago.

Hygiene; Growth and Nutrition; Public Health

PREDICTING PUBERTY. CHARLES D. FLORY, Child Development **6**:1 (March) 1935.

In an attempt to find a measure by which the probable onset of puberal changes in a given child could be predicted, Floray examined the clinical and roentgenographic records of about eighty girls who had been observed annually for a period of ten years. The data revealed that puberty is related to physical size and osseous development. Although any physical measure appears to have some relationship to the onset of pubescence, measurements of the head are less valuable than measurements of the chest, and widths of the hips are more valuable than dimensions of the chest as predictors of the first menstruation. There is a closer relationship between osseous development and puberty than between physical size and puberty. The author believes that the time of appearance of the sesamoid bone on the distal end of the first metacarpal bone is the simplest and best single predictor of puberty in girls, for the data showed that no girl had menstruated the roentgenogram of whose hand showed the absence of the sesamoid bone that usually appears about two years before puberty.

ABRAMSON, New York.

SOME INFLUENCES OF A HEALTH-EDUCATION PROGRAM DURING THE ELEMENTARY SCHOOL YEARS. CAROLYN HOEFFER and MARTHA C. HARDY, Element. School J. **25**:368 (Jan.) 1935.

This program was developed in the public schools of Joliet, Ill., and was initiated in the second and third grades. The special contribution was made by a staff of child specialists, among whom were a pediatrician, a psychologist and health educators from the Elizabeth McCormick Memorial Fund. Four hundred and nine pupils were observed, the average age being 8 years. The results, on the whole, indicated improvement in the physical condition of the pupils who participated in any part of the program, the children having the most extensive contacts with health education showing the greatest improvement.

SANFORD, Chicago.

THE RÔLE OF HEALTH IN THE CHILD'S DEVELOPMENT. CAROLYN HOEFFER and MARTHA C. HARDY, Element. School J. **25**:423 (Feb.) 1935.

In a study of four hundred and nine children for a period of three years it was found that the number of very healthy children usually exceeded that of children said to be in fair health by as much as the number of the latter, in turn, exceeded that of children in poor health. Thus, it would seem highly probable that vigorous health during the elementary school years plays a significant rôle in wholesome development.

SANFORD, Chicago.

HEIGHT AND WEIGHT OF CHILDREN OF THE DEPRESSION POOR. CARROLL E. PALMER, Pub. Health Rep. **50**:1106 (Aug. 16) 1935.

This study deals with the relative change in height and weight during 1929 to 1933 of urban children from (1) families that remained in comfortable economic circumstances during the entire period, (2) families that remained poor and (3) families that were comfortable in 1929 but that had become poor by 1933. This material comprised 5,000 families and 5,400 children. It was shown that the weight of the young children from the group that had become poor was 2 per cent lower than that of the young children as a whole. SANFORD, Chicago.

THE PLACE OF SUN-BATHING, SEA-BATHING, AND OPEN-AIR EXERCISE IN GROWTH AND DEVELOPMENT. K. R. COLLIS HALLOWES, Brit. J. Phys. Med. **10**:27 (June) 1935.

The beneficial and harmful effect of thalassotherapy are discussed. The necessity for the individualization of this form of therapy is emphasized.

HARTMAN, Cleveland.

INFANT PROTECTION IN MADAGASCAR AND TOGO. A. THIROUX, Rev. méd.-sociale de l'enf. **3**:43 (Jan.-Feb.) 1935.

The Union des Femmes de France (Union of French Women) in Madagascar, founded by the wife of General Gallieni at the time of the conquest, early established a kindergarten in the capital of Madagascar. Since 1922 Mme. Oliver, wife of the governor-general, has actively interested the Union of French Women in infant welfare, and with the collaboration of the Health Service she has organized a large dispensary for the feeding, bathing and treatment of infants. The number of visits rose from 12,000 in 1922 to over 77,000 in 1933, on the basis of 24,399 patients. The dispensary was enlarged in 1927, and four native physicians were employed to aid the European directing physicians.

In 1933 the following diseases were noted most frequently at the clinic: malaria, in 6,952 patients on 24,888 visits; infections of the respiratory tract, in 8,426 patients on 24,023 visits; infections of the gastro-intestinal tract, in 5,481 patients on 12,207 visits, and congenital syphilis, in 571 patients on 8,169 visits.

To lower the number of infections due to the chill weather during the dry season on the plateaus, the union has distributed each year many thousands of garments.

Medical Commandant Huot noted a mortality of 20 per cent in a group of 276 infants in which there were regular observations on feeding, whereas without this service about 70 per cent undoubtedly would have died. Because the aforementioned care of sick babies was so inadequate and the mothers refused to take their babies to the general hospital, it was necessary to build a small pavilion adjoining the dispensary. An immediate success, it had to be augmented by a larger second unit, and a third is needed. In 1933 11,216 hospital days were accorded 1,463 babies, 31 of whom were permanently hospitalized.

By an order of Aug. 2, 1934, a school of visiting nurses in association with the Institute of Social Hygiene is to be created. With these facilities Tananarive finds itself in advance of other colonial capitols in the protection of public health. However, in the districts throughout Madagascar progress is not as great as in the capital.

Similar work is carried on in Togo by the Union of French Women, aided by the government. Dispensaries have been established, where the infants are given a medical examination by a physician and trained women helpers, who refer to the physician any babies who are sick or not gaining properly. The number of visits to these centers rose from 1,083 in 1924 to 40,884 in 1933. The midwives and nurses also visit the homes and refer sick children to the physicians. A social service is established in the capital Loiné. SHAW, Evanston, Ill.

Prematurity and Congenital Deformities

CHONDRODYSTROPHIA FETALIS: A ROENTGEN STUDY OF FOUR CASES; TWO IN FATHER AND DAUGHTER, EMPHASIZING THE EPIPHYSEAL CHANGES AND VARIANTS. PAUL O. SNOKE, Am. J. Roentgenol. **29**:31 (Jan.) 1933.

Snoke cites Bangson, who traced chondrodystrophia foetalis through five generations, in two of which the parents were normal adults; the sequence adhered to the mendelian law. The etiology is discussed, and four cases in which roentgen studies were made are reported. An attempt is made to correlate the clinical and histologic picture. Roentgenograms of young persons afford the best method of study. The author believes that the three types of Kaufmann—hypoplastic, hyperplastic and malacic—may be present in the same patient, one process predominating. This accounts for the many variable findings in the reported cases. In the same person the several groups of bones may vary in the severity of their involvement; e. g., the bones of the wrist may be more seriously affected than those of the knee, the roentgenograms revealing the results of a differing histologic picture.

A bibliography and roentgenograms are included in the article.

STULIK, Chicago.

PILONIDAL CYSTS AND SINUSES. LESTER BREIDENBACH and H. LYNN WILSON, Ann. Surg. **102**:455, (Sept.) 1935.

Pilonidal cyst is a congenital malformation occurring in the sacrococcygeal region, characterized by acute and chronic inflammation, the presence of tufts of hair, occasional islets of squamous epithelium and foreign body giant cells. The authors analyze 288 cases.

These cysts occur in some degree in about one third of all new-born infants, but the condition appears in only 3 per cent of adults. Itching, pain on sitting or walking and discharge of pus are the predominant symptoms.

The generally accepted treatment is complete surgical excision, and since there is infection in all these cases, any method involving closure of the wound is contraindicated. Spinal, caudal and local anesthesias are definitely contraindicated.

BANTIN, Omaha.

CONGENITAL STENOSIS OF THE DUODENUM TREATED BY GASTRO-ENTEROSTOMY. DENIS BROWNE, Proc. Roy. Soc. Med. **28**:1335 (Aug.) 1935.

A case of congenital stenosis of the duodenum in a boy of 18 months is reported. At 14 days of age he began to vomit. The vomiting was projectile in type. There was visible peristalsis, and a large tumor was felt under the right rectus muscle. Dr. Ellis suggested a diagnosis of duodenal stenosis, which was confirmed at operation. A brief description of the operation concludes the report.

WILLIAMSON, New Orleans.

CRANIOFACIAL DYSOSTOSIS: ANATOMIC EXAMINATION. H. GRENET, J. LEVEUF and P. ISAAC-GEORGES, Bull. Soc. de pédiat. de Paris **32**:343 (June) 1934.

A girl, 21 months old, whose congenital deformity was described in a previous communication, showed bilateral papilledema and progressively more marked visual impairment. A right cranial decompression was performed, and a small opening in the dura was made. The child went into collapse and died. Necropsy revealed no abnormalities other than those observed in the cranium. There were a marked prominence of the skull at the site of the anterior fontanel and a slight crest extending posteriorly along the sagittal suture. The cranial vault was very thin, and there was marked furrowing of the internal surface of the vault and on the base of the skull. There were no visible sutures in the vault. The roofs of the orbits were prominent. The sella turcica was normal. The anterior orifice of

the optic canal was narrowed, owing to a small lesser wing of the sphenoid on both sides, and this accounted for mechanical strangulation of the optic nerve. From the operation and the necropsy it was learned that there was no increase in the intracranial pressure, that the sutures were absent in the vault of the skull and that the blindness was due to strangulation of the optic nerves at the anterior orifices of the optic canals. The operation indicated in such cases is simply the removal of a piece of the superior wall of the orbit as far as the superior border of the optic canal to reduce the strangulation of the optic nerve. Five operations of this nature have been reported by a German surgeon, in two cases bilateral and in one case unilateral. The results were good; i. e., the progress of optic atrophy was arrested.

BENJAMIN, Montreal, Canada.

FETAL AMINO-ACIDEMIA. GIUSEPPE SANNICANDRO, Fisiol. e med. **6**:413 (June 20) 1935.

In fifteen infants born spontaneously after normal pregnancies the acid content of the blood was determined by a modified Van Slyke technic which effects disalbumination of the blood. The result showed the amino-acid content of the blood of the fetus to be constantly in excess of that of the blood of the mother. The difference varies between 1.15 and 2.09 mg. per hundred cubic centimeters, averaging 1.54 mg. The author's views regarding the aminonitrogen content of the fetal blood are set forth also in respect to the source of fetal aminonitrogen, which, he believes, passes through the placenta in accordance with the law of osmosis. The presence of a larger amount of animo-acid in the fetal blood than in the maternal blood is ascribed to a biologic process in the intra-uterine life evidently connected with a special function of the fetal liver.

VINTON, New York.

ERROR IN DIAGNOSIS IN A CASE OF THE KLIPPEL-FEIL SYNDROME. L. RIBO RIUS, Paidoterapia **13**:1113 (March) 1935.

An interesting case of the Klippel-Feil syndrome is presented in which the diagnosis of osseous tuberculosis had been made. The most important features of the syndrome are absence of pain and nervous disorders and presence of congenital rudiments. This picture helps to differentiate the stiffness of the neck from Pott's disease. The roentgenogram showed that the sixth and seventh dorsal vertebrae were in the form of steps and that the third cervical vertebra was smooth and flat, which produced the limitation of motion and stiffness of the neck.

HERRON, Spokane, Wash.

New-Born

HYPERVENTILATION IN THE TETANY SYNDROME OF THE NEW-BORN, WITH SPECIAL REFERENCE TO THE CYANOTIC SPELL. W. RAY SHANNON, Arch. Pediat. **52**:501 (Aug.) 1935.

Hyperventilation is thought to play a significant rôle in the development of tetany in many new-born infants. Three causes tending to produce hyperventilation are: (1) physiologic developments in the lungs, making each respiration more efficient than the one preceding; (2) anoxemia; (3) deficiency of the ionic calcium. Hyperventilation is suggested as the connecting link between the tetany syndrome and pathologic states that interfere with the nervous control, mechanics or chemistry of respiration. As such it explains the confusion that exists in the differential diagnosis between the tetany syndrome and conditions such as cerebral hemorrhage, atelectasis and bronchial obstruction.

Shannon believes that many symptoms formerly attributed to these conditions are symptoms of tetany. Cyanosis in the new-born is in many instances a mani-

festation of hyperventilation and depends on hypersensitivity and not on primary depression of the respiratory center. Calcium therapy plays an important rôle in the treatment of hyperventilation and, therefore, of the cyanotic spells.

The criteria on which hyperventilation is diagnosed are the clinical picture, the reactions of the urine and the response to therapy. "Acute symptoms and alkaline urines + treatment = cure and acid urines." Eight cases and the treatment are reported in support of Shannon's theory as to the cause of tetany in many cases.

WADDELL JR., University, Va.

OPHTHALMIA NEONATORUM TREATED WITH GONOCOCCUS FILTRATE (CORBUS-FERRY). B. P. STORTS, Arch. Pediat. **52**:567 (Aug.) 1935.

A case of ophthalmia neonatorum is reported in which the patient was treated with the Corbus-Ferry gonococcus filtrate. WADDELL JR., University, Va.

ICTERUS NEONATORUM. NORMAN BOOK, Canad. M. A. J. **33**:269 (Sept.) 1935.

Acting on the suggestion of Ylppö that physiologic jaundice is a benign process which may become pathologic when the blood content becomes excessive, Book compared two groups of two hundred babies each. In one group the cord was tied immediately, and in the other the cord was tied after all pulsation had stopped. It was estimated that the babies in the second group received from 40 to 50 cc. more blood than those in the first group. From these experiments it was concluded that the immediate tying of the cord resulted in a definite decrease in the incidence and degree of jaundice, without any disadvantage to the baby.

MOORE, Omaha.

LIMITATIONS OF USE OF SILVER NITRATE IN PREVENTION OF OPHTHALMIA NEONATORUM. L. LEHRFELD, J. A. M. A. **104**:1468 (April 27) 1935.

A survey of the records of the health department in Philadelphia for the past fifteen years shows that ophthalmia neonatorum has not decreased. In fact, the incidence is twenty-two times that recorded by Credé. A study of the methods used in six institutions revealed that prophylaxis was being carried out, but that the Credé method of prophylaxis as originally described was not being used or that the germicide has been relied on too much. Lehrfeld recommends more active effort in the prenatal treatment of gonorrhea and the compulsory reporting of all cases of ophthalmia neonatorum, as well as the compulsory reporting six weeks later of the results of the treatment. He also recommends a different technic for the care of the eyes during the first few days of life.

BONAR, Salt Lake City.

VALUE AND LIMITATIONS OF SPINAL PUNCTURE IN CEREBRAL HEMORRHAGE OF THE NEW-BORN. ABRAHAM LEVINSON, J. A. M. A. **104**:2243 (June 22) 1935.

Fresh blood in the cerebrospinal fluid of the new-born, especially if it persists in successive portions of the fluid, suggests the presence of cerebral hemorrhage, but it is not pathognomonic of the condition, for the blood may come from trauma at the time of puncture. The finding of clear fluid does not exclude hemorrhage, especially if it is in the ventricles. Xanthochromia associated with a positive benzidine reaction indicates cerebral hemorrhage, but without such a positive reaction xanthochromia may be due only to meningeal congestion. Levinson divides the symptoms of cerebral hemorrhage during the neonatal period into two types—irritative and somnolent. The irritative type is characterized by restlessness, a high-pitched cerebral cry, moaning and a pained expression. The extremities may or may not be spastic immediately after birth, and facial paralysis and nystagmus may or may not be manifested at this time. A bulging anterior

fontanel is of frequent occurrence. In the somnolent type there are apathy, a subnormal temperature, dysphagia, fleeting cyanosis and sometimes a depressed fontanel. All cases of cerebral hemorrhage are not of the same type clinically or pathologically, and the hemorrhage may be absorbed without leaving a scar without treatment. Levinson believes that in hemorrhage of the somnolent type spinal puncture is unnecessary and, if done, should not be repeated. In hemorrhage of the irritative type, spinal puncture should be done for therapeutic purposes and may even be repeated. Rest is essential; nursing should be prohibited, and feedings should be small. For dehydration, physiologic solution of sodium chloride should be given subcutaneously, and for fleeting cyanosis, oxygen or oxygen and carbon dioxide should be administered. The body heat should be maintained, and blood should be given intramuscularly. Sedatives such as sodium amytal or sodium bromide may be administered for convulsions, and the subcutaneous administration of a hypertonic solution of sodium chloride or a 10 to 15 per cent solution of dextrose is of value in reducing the intracranial pressure.

BONAR, Salt Lake City.

THE SIGNIFICANCE OF THE SHAPE OF THE FOETAL HEAD IN THE MECHANISM OF LABOUR. ERIK RYDBERG, J. Obst. & Gynaec. Brit. Emp. **42**:600 (Aug.); 815 (Oct.) 1935.

A comprehensive discussion of the most important theories which have been advanced to explain the mechanism of labor is presented, and the conclusion is reached that no fully satisfactory theory has hitherto been advanced.

Rydberg believes that the usual movement of the fetal head during labor is due to its shape and considers the birth canal a deformable curved tube of homogeneous elastic material. He has made a careful study of the shape of the head and describes it as decidedly and characteristically asymmetrical, with the bulk of the mass situated above the mento-occipital diameter. The mechanism of labor, with the shape of the head as the determining factor, is described in various types of deliveries.

ADAIR and POTTER, Chicago.

EPIDEMIC PEMPHIGUS OF THE NEWLY BORN (IMPETIGO CONTAGIOSA ET BULLOSA NEONATORUM). C. H. WHITTLE, Lancet **1**:1323 (June 8) 1935.

During July and August 1931, nine cases of pemphigus of the new-born came under the author's observation. Two of the patients died. The causative organism appeared to be Staphylococcus pyogenes-aureus.

Whittle suggests the following classification: (1) exfoliative dermatitis; (2) vesicular and bullous lesions, in which extensive coalescence and exfoliation do not occur, and (3) crusted lesions. Under the first classification are the majority of severe and fatal cases; under the second, the majority of all the cases, and under the third, the rare cases.

The Cambridge epidemic illustrates spread of the disease by three avenues. In eight cases infection was almost certainly spread by Nurse A, who was a carrier; in one case it was apparently contracted from Nurse B, who became a carrier by contact, and one child was reinfected by his own clothes after being discharged cured.

In the seven cases in which recovery occurred the average duration was twenty-two days. The organism is carried on the skin of the carrier and is conveyed by direct contact to the skin of the infant.

There is remarkably little constitutional reaction. The essentials of the treatment are cleansing and dressing with a mild antiseptic.

LANGMANN, New York.

LIPOGRANULOMATOSIS AND ADIPONECROSIS IN THE SUBCUTANEOUS TISSUE OF THE NEW-BORN. S. MOSCHINI, Riv. di clin. pediat. **33**:906 (Aug.) 1935.

The patient was born one month after term. Labor was difficult; there was a premature rupture of the membranes, and the application of forceps had been

necessary. The child was apparently dead at birth but revived following artificial respiration.

At 4 months of age the child had numerous symmetrical subcutaneous areas of induration, especially over the back, shoulders, neck and thighs. After a biopsy of tissue from one of the swellings, a diagnosis of lipogranuloma of the subcutaneous tissue was made. It is probable that at first there was necrosis of the fat tissue (adiponecrosis); this was followed by a granulomatous infiltration containing fibroblasts, plasma cells, monocytes and giant cells. One of the areas became infected during the child's stay in the hospital, and considerable pus was obtained on incision.

HIGGINS, Boston.

RITTER'S DISEASE AND EPIDEMIC PEMPHIGUS. J. ROBALINHO CAVALCANTI, J. de pediat., Rio de Janeiro **2**:361 (Aug.) 1935.

A case of Ritter's disease occurred shortly after a case of epidemic pemphigus, in an infant in the same institution. This led Cavalcanti to believe that Ritter's disease is not an individual clinical entity but that it is simply a malignant form of pemphigus.

SANFORD, Chicago.

Acute Contagious Diseases

PHYSIOLOGIC CONDITIONING OF THE SCHICK REACTION. J. GAUTRELET and M. GAUTRELET, Presse méd. **43**:961 (June 15) 1935.

The authors have studied the rôle of the vegetative nervous system and of the circulation in the Schick reaction, using shaved guinea-pigs. They found that the reaction may be delayed and markedly attenuated by the injection of sparteine, epinephrine hydrochloride, acetylcholine and solution of posterior pituitary. The opposite effect was produced by the administration of histamine and, to some extent, by the potassium salts. The effect of the latter could be offset by calcium chloride. This bears out the finding of Eckart that the potassium salts produce vasodilatation and calcium salts produce the reverse and that an equilibrium of the salts is without effect. These findings seem to indicate that capillary tone plays an important part in the conditioning of the Schick reaction. It has been shown by a number of authors that the toxin of diphtheria produces dilatation of the peripheral arterioles and that the circulatory collapse, cardiac failure and concentration of the blood due to extravasated plasma are comparable to histamine shock. It is well to note, also, that in diphtheritic circulatory failure the action of epinephrine is weak but posterior pituitary may benefit the blood pressure.

The authors are not promoting the theory that the Schick reaction is due to the liberation of a histamine-like substance in the capillary walls, but they are interested in establishing the connection between the vegetative nervous system and the biologic factor in immunity.

BIEKER, St. Petersburg, Fla.

RATIONAL SERUM THERAPY IN DIPHTHERIA. A. I. JAROTZKY, Progrès méd., June 29, 1935, p. 1117.

Jarotzky believes that serum therapy should be repeated in diphtheria as long as signs of toxicity persist. This usually means a daily or possibly a more frequent dose of from 10,000 to 20,000 units of antitoxin until from six to eight doses have been given. Signs of myocardial damage should be met by injections of serum. The serum should have a titer of not less than 750 units of antitoxin per cubic centimeter.

Satisfactory results have been obtained by this method in 915 cases of diphtheria. The lower mortality in cases of laryngeal diphtheria is particularly striking.

LESLIE, Evanston, Ill.

COMBINED VACCINATIONS. L. TANON and H. CAMBESSÉDÈS, Rev. franç. de puériculture **2**:298 (Nov.) 1934.

It has been shown that if diphtheria toxoid and typhoid vaccine are given together the efficacy of the toxoid is augmented and that of the vaccine is not decreased. Likewise, tetanus anatoxin and diphtheria toxoid can be administered together effectively. In circumstances in which immunization against tetanus or typhoid is indicated for the child between 1 and 2 years of age the authors recommend that it be given in combination with diphtheria toxoid.

CRANE, Chicago.

FIFTIETH ANNIVERSARY OF THE DISCOVERY OF ANTICHOLERA VACCINATION. MARTÍNEZ VARGAS, Med. de los niños **36**:65 (March) 1935.

This article commemorates the fiftieth anniversary of Ferran's discovery of a vaccine for the treatment of cholera. Jenner's discovery of smallpox vaccine was casual, while Ferran's discovery was the result of actual experiment, inspired by the idea that an inoffensive attenuated infection would protect against a more severe infection. The announcement startled the world like that of the discovery of antidiphtheritic serum. This generation will never realize the great importance of cholera and the significance of the disease as a barrier to commerce. The mortality was appalling. From 1817 to 1840 443 epidemics were recorded in India at the mouth of the Ganges and in Brahmaputra, resulting in 18,000,000 deaths. The disease was rapidly fatal, producing within a few hours after its invasion vomiting, incessant diarrhea, great prostration, burning thirst, sunken eyes, rapid emaciation, chills, cramps and inevitable death.

Five epidemics swept over Europe. The first, from 1830 to 1837, caused 100,000 deaths; the second, from 1848 to 1851, 110,000 deaths, and the third, from 1851 to 1855, 143,478 deaths.

The effectiveness of Ferran's work in checking this scourge is attested by his contemporaries, Koch, von Behring, Kitasato, Roux and Metchnikoff.

DWYER, Kansas City, Mo.

SEROTHERAPY OF DIPHTHERIA. H. KLEINSCHMIDT, München. med. Wchnschr. **82**:1143 (July 19) 1935.

That the efficacy of specific serotherapy has been seriously questioned by many physicians in Europe is emphasized in the comprehensive article which Kleinschmidt has written in support of the treatment of diphtheria with antitoxin. He cites statistics from observations of Bókay over a long period of years. From 1895 to 1897 the mortality in cases of faucial diphtheria was 18.1 per cent, and in cases of laryngeal diphtheria, 40.9 per cent. In the years 1929 and 1930 the mortality rate for patients with faucial lesions was 6.6 per cent, and for those with laryngeal lesions it was 28.9 per cent. It is interesting to note the difference in the type of infection in various periods. In 1897 there was about an equal number of patients with laryngeal and faucial diphtheria, whereas in 1930, 87.7 per cent had faucial diphtheria, and 12.3 per cent had laryngeal diphtheria. This shift to the less serious form of the disease is largely due to the effect of antitoxin, according to Kleinschmidt. Before the use of antitoxin the lesion in a great many cases spread from the pharynx to the larynx. This occurs infrequently in patients treated with serum, a fact which recently has been overlooked.

Kleinschmidt prefers to consider antitoxin as a preventive rather than a curative agent. It prevents the continued deleterious effect of the toxin. This is borne out by the fact that the earlier in the disease antitoxin is given the lower the mortality. The destructive action of the toxin may continue from three to six or even twenty-four hours after the injection of antitoxin, as was shown by Schick. This explains the spread of the membrane and the continued toxemia in some patients treated with serum.

BRAHDY, Mount Vernon, N. Y.

BLANCHING PHENOMENON IN SCARLET FEVER, CALCIUM BLANCHING PHENOMENON, PSEUDOBLANCHING PHENOMENON. F. GERTH and F. TRAUTMANN, München. med. Wchnschr. **82**:1188 (July 26) 1935.

The blanching phenomenon in scarlet fever is produced by the intracutaneous injection of from 0.3 to 0.5 cc. of blanching serum into the area of the exanthem. A positive reaction consists of an area of blanching 1 inch (2.54 cm.) or more in diameter, which occurs in from six to eight hours. It is specific. The calcium blanching phenomenon is due to a vasomotor action of the calcium salt. In the blanching following the injection of a calcium salt there is a red papule in the center of the blanched area, with a bluish-red area surrounding the blanched zone.

BRAHDY, Mount Vernon, N. Y.

EFFECT OF RECTAL INJECTION OF ETHER ON THE BLOOD PICTURE IN PERTUSSIS. K. OKUTANI, J. Pediat. (Tokyo), no. 421, June 20, 1935, p. 861.

After the rectal injection of ether in fifteen cases of whooping cough the author noted a relative decrease in lymphocytes and a corresponding increase in neutrophils. The change in the blood picture coincides with the clinical improvement.

KATO, Chicago.

CLINICAL AND SEROTHERAPEUTIC STUDIES ON THE PREPARALYTIC STAGES OF POLIOMYELITIS ON THE BASIS OF EXPERIENCE DURING THE EPIDEMIC IN SKIVE DISTRICT IN 1933. SKAT BAASTRUP, Acta med. Scandinav. **85**:262, 1935.

This fifty-two page article is based on a study of 120 cases in a single epidemic, all personally observed by the author.

Early diagnosis in the preparalytic stage is essential if beneficial results from convalescent serum are expected. In this stage the diagnosis must be based on the presence of all the three cardinal symptoms: (1) elevation of temperature (at the moment or within the last few days); (2) the typical appearance of the patient, i. e., congestion and cyanosis, with circumoral pallor (in some cases, paleness and cyanosis) associated with drowsiness; (3) meningeal symptoms (spinal stiffness was present in all the cases, but stiff neck in only twenty-one cases).

Other symptoms, not essential but making the diagnosis more certain, are: (*a*) Pathologic changes in the cerebrospinal fluid—a high cell count or an increased amount of globulin. Such changes were found in 87 per cent of the cases (in five cases, in spite of daily examination, the spinal fluid was normal). (*b*) Headache. This was present in 82 per cent of the cases. (*c*) Abnormality of tendon reflexes. This was present in 58 per cent of the cases. (*d*) Hyperesthesia and neuralgic pain. These were present in 33 per cent of the cases. (*e*) Vomiting. This occurred in 31 per cent of the cases. (*f*) Kernig's sign. This was present in 23 per cent of the cases. (*g*) Absence of abdominal reflexes. This was noted in 17 per cent of the cases. The differential diagnosis from influenza and meningitis is discussed.

Serum treatment was given in twenty-four cases during the preparalytic stage. In seven of these Pettit's immune horse serum was used, without any effect. In seventeen cases convalescent serum seemed to help the general condition, though its prophylactic effect against paresis could not be established.

KAJDI, Baltimore.

A SMALL NOSOCOMIAL EPIDEMIC OF EXANTHEMA SUBITUM. H. RYDÉN, Acta pædiat. **17**:498, 1935.

Considerable difference of opinion exists concerning the etiology of the exanthematous disease of infants and young children first described by Zahorsky in 1910 under the title "roseola infantum" and which is now commonly known as "exanthema subitum." American authors, in particular, have expressed the convic-

tion that the disease is not infectious but is an expression of allergy toward certain food substances. Japanese and German authors doubt that exanthema subitum is a disease sui generis; they regard it as an atypical form of influenza. Certain features of the disease suggest that it may be an aberrant form of rubeola.

During the autumn of 1933 Rydén had occasion to observe eight cases of an exanthematous disease which possessed the clinical characters of exanthema subitum. Scarlet fever, rubeola, erythema infectiosum, erythema toxicum and influenza were considered in the differential diagnosis and were excluded to the author's satisfaction. There had been no recent changes in the patients' diet. The epidemic took place within a period of about four weeks in the Flensburg Children's Hospital, Malmö, Sweden. It was not preceded or followed by cases of similar illness, and it occurred at a time when the state of health of the community was excellent.

On the basis of a critical analysis of the features of the epidemic, Rydén draws the conclusion that exanthema subitum is a distinct etiologic and nosographic entity and that it is contagious and therefore probably infectious. The causal agent is unknown.

McCune, New York.

Acute Infectious Diseases

Control of Rabies in New York City. Robert Olesen, Pub. Health Rep. **50**:1087 (Aug. 16) 1935.

This article is difficult to abstract and should be read in full by any one interested in the subject, as it is excellent. It should be especially interesting for those who wish information as to the cost of the control of rabies in a large city and the morbidity, and mortality. The part on public education should be of value to health officers, as Olesen states, "If the owners of biting dogs were sufficiently penalized there would be a marked and rabid reduction in occurrences."

Sanford, Chicago.

Epidemic Jaundice in Children. M. A. Moore, West Virginia M. J. **31**:198 (May) 1935.

Two small groups of cases are reported. All these cases occurred in children in the fall during the prevalence of colds; all the patients recovered.

This condition is different from Weil's disease, which is due to Leptospira icterohaemorrhagiae, and occurs largely in adults. It also differs from catarrhal jaundice. The probable cause of the disease is an air-borne organism or virus, which finds entrance through the upper respiratory tract.

The symptoms, treatment, epidemiology and other features are discussed briefly.

Shawkey, Charleston, W. Va.

Aetiology of Acute Rheumatism: Experimental Evidence of a Virus as the Causal Agent. B. Schlesinger, A. G. Signy and C. R. Amies, Lancet **1**:1145 (May 18) 1935.

This study is based on the examination of the pericardial fluid in seven cases of acute rheumatism that ended fatally. The pericardial fluid was removed with aseptic technic within twelve hours after death. To serve as adequate controls eight pericardial exudates and two pleural exudates obtained from nonrheumatic persons were investigated in a similar manner. The authors found the following:

1. The deposits obtained by high speed centrifugation of the pericardial fluid from the patients with acute rheumatic pericarditis contained particles which morphologically resembled virus elementary bodies. Similar bodies were found in the deposit obtained from the pleural exudate in association with rheumatic pneumonia.

2. Suspensions of these bodies in physiologic solution of sodium chloride containing a small amount of formaldehyde were agglutinated by the serums of patients suffering from and successfully resisting an acute rheumatic infection. The serums of patients in whom the infection was quiescent failed, as a rule, to agglutinate these suspensions. Completely negative reactions were also obtained with the serums of normal persons and of patients suffering from various nonrheumatic infections.

3. On the basis of the evidence just summarized, it is suggested that the bodies found in pericardial exudates represent the actual infective agent of acute rheumatism.

4. The importance of streptococcic infection as a factor in the etiology of the disease is recognized. It is suggested that the lowered resistance produced by such infections enables the virus to enter the body or, if the virus is already lying latent in the tissues, allows it to assume an active character.

LANGMANN, New York.

A NOTE ON THE INCIDENCE OF RHEUMATIC INFECTIONS IN AUSTRALIA. E. L. COOPER, M. J. Australia **1**:714 (June 8) 1935.

Cooper's study shows that rheumatic infections are more common and more severe in southern Australia than in the tropical north. It also shows that contrary to the contention that rheumatic fever is unknown in the tropics, acute rheumatic fever occurs not infrequently in tropical (northern) Australia. Chronic rheumatoid arthritis, however, seems much less common in the northern states than acute rheumatism.

GONCE, Madison, Wis.

A DIETETIC STUDY OF CASES OF JUVENILE RHEUMATIC DISEASE. EDWIN C. WARNER, FRANK G. WINTERTON and M. L. CLARK, Quart. J. Med. **4**:277 (July) 1935.

This investigation was designed to ascertain whether a dietetic deficiency or other factors existed which might lower the general resistance of children to rheumatic fever.

A record of the food consumed by rheumatic families as a whole was compared with that of food consumed by control families of the same social stratum. Individual likes and dislikes were taken into consideration. A detailed record of the actual food consumed by a small number in each group over a period of two days was obtained. These results were compared with the diets of children in localities where the evidence of rheumatic fever was low. Expenditures on food and rent are discussed.

It was found that the rheumatic group consumed more total protein, as well as more animal protein, more total animal fat and more carbohydrate than did the control group. The caloric intake of the rheumatic families indicated no deficiency. The authors point out that the lowest intake of fresh cow's milk corresponded with a high proportion of rheumatism. The potato ration was higher in the rheumatic group, this being due in part, according to the authors, to a craving for potatoes shown by the rheumatic children. The consumption of fresh fruit and vegetables was much higher for the rheumatic children than for the controls, which is a point of interest, particularly in view of the suggestion that vitamin C deficiency is related to the rheumatic diathesis.

The authors conclude that any one of the dietary factors investigated could not be incriminated as a contributory cause for rheumatism occurring in certain families and certain children. They point out that the consumption of animal protein and of dairy products by rheumatic children and by the controls of the same social stratum was low and that the intake of carbohydrate, particularly in the form of potatoes, was high.

BRADFORD, Rochester, N. Y.

Chronic Infectious Diseases

A Series of Eighty-Four Cases of Pulmonary Tuberculosis in Children Aged 0-15 Years. J. Reginald Beal, Tubercle **16**:452 (July) 1935.

In this group of cases the incidence of pulmonary tuberculosis on the basis of age and sex was as follows: from birth to 5 years of age, thirteen for boys and seven for girls; from 6 to 10 years, ten for boys and seventeen for girls, and from 11 to 15 years, seventeen for boys and twenty for girls, or forty for boys and forty-four for girls, of all ages.

Of the cases in which tubercle bacilli were present in the sputum, eight were in boys and eighteen in girls. Of the cases in which no bacilli were found in the sputum, thirty-two were in boys and twenty-six in girls.

On the basis of the type of the disease the cases could be classified into four groups: (1) Fibrocaseous tuberculosis, in which the type of the disease approximated that of the adult and the course was chronic with an attempt at repair, forty-one cases. Of this number sixteen patients died, and thirteen remained in institutions; in nine cases the disease was stationary and not arrested. In one case the disease appeared to be quiescent, and two of the patients were lost sight of. (2) Infiltrative type, twenty-two cases. Nine of these patients died, and three were in institutions; in six cases the disease was not arrested, and in four it was quiescent. (3) Tuberculosis with pleural effusion. The immediate outlook in seventeen cases appeared to be favorable. Only one death occurred; the disease was quiescent in nine cases and improved, but not arrested, in five; one patient remained in the institution, and one had been lost sight of. (4) Hilar tuberculosis, the smallest group, consisting of four cases. The prognosis is good.

Bacilli appeared in the sputum in 40.9 per cent of the girls, as compared with 20 per cent of the boys. In 48.8 of all the cases the disease was of the adult type, with a correspondingly bad prognosis. Eugene Smith, Ogden, Utah.

Syphilis Tardive Simulating Tuberculosis in Childhood: Vaccination with BCG; Tuberculin Allergy. José M. da Rocha and Arlindo de Assis, Arch. de méd. d. enf. **38**:335 (June) 1935.

A case of delayed syphilis in a boy of 4 years, which illustrates the difficulties of differential diagnosis and the supreme value of the tuberculin test, is reported from the clinic of pediatrics of the University of Rio de Janeiro.

The patient was admitted with a history of cough for two years, accompanied by abundant expectoration, occasional febrile attacks and disturbance of sleep. The family history was normal except for several miscarriages; six brothers and sisters were in good health, and the boy himself had enjoyed normal health for two years after birth.

Examination showed great emaciation, with marked dehydration, dry, pale skin, enlarged lymph nodes in the cervical, submaxillary, axillary and crural regions, subnormal temperature, cold extremities, coryza and a productive cough. There was a diminished vesicular murmur over the entire right lung, with an amphoric souffle immediately below the clavicle on this side, giving the characteristic cracked pot phenomenon. Percussion showed normal resonance. The liver was palpated 1 fingerbreadth below the costal arch, but the spleen could not be felt. Examination of the sputum and feces failed to reveal the Koch bacillus, and subsequent inoculation of guinea-pigs revealed no manifestation of tuberculosis. The blood picture was essentially that of secondary anemia, and the Wassermann reaction was strongly positive.

A few weeks after admission to the clinic the abdomen became markedly distended; both the liver and the spleen were enlarged, and the collateral circulation was readily noted. The patient's general condition, however, was greatly improved, and the weight steadily increased. The Mantoux test, repeated on four occasions with doses increasing from 0.01 to 1 mg., gave consistently negative

results. With the conventional treatment for syphilis there was gradual amelioration of all the symptoms, and the boy was discharged as recovered in four and one-half months.

AMESSE, Denver.

TUBERCULOUS ALLERGY AND SO-CALLED PHLYCTENULAR KERATOCONJUNCTIVITIS. N. COLOMBA, Ann. di ottal. e clin. ocul. **63**:437 (June) 1935.

Colomba examined thirty-one patients with reference to their reactions to tuberculous antigens. The tests employed were (1) intradermal tests with a 1:1,000 dilution of old tuberculin; (2) complement-fixation tests on the blood; (3) examination of the urine for its content of tuberculous antigens, and (4) examination for other symptoms of tuberculosis, including roentgenography of the chest. The intradermal reactions were positive in 96.6 per cent of the cases. Complement-fixation tests gave positive results in only seven cases, or 22.54 per cent. Antigens were found in the urine in six cases, or 19.32 per cent. Roentgen examination of the chest showed active tuberculosis in seven cases and signs of tuberculosis in twenty-four.

Colomba believes that this demonstrates the tuberculous nature of phlyctenular keratoconjunctivitis in the sense that a previous tuberculous infection has sensitized the patient to tuberculous products. The recent views on the interpretation of tuberculin reactions and the relation of allergy to tuberculosis are reviewed.

GIFFORD, Chicago. [ARCH. OPHTH.]

THE TUBERCLE BACILLUS IN THE URINE OF TUBERCULOUS CHILDREN. E. PEZZA, Pediatria **43**:789 (July) 1935.

As a result of the detailed study of fifty-one cases of known tuberculosis in children, the author states that the tubercle bacillus is found in the urine only with extreme rarity, unless the tuberculous focus is in the kidney. Since the detection of such lesions is difficult with ordinary means, a thorough search for the organism in the urine is to be made in all cases.

SIGNORELLI, New Orleans.

PHRENECTOMY AS A FORM OF TREATMENT IN TUBERCULOSIS. OSORIO M. ARTURO, and SAYMON O. JOSÉ, Arch. Hosp. de Niños Roberto del Rio **5**:1 (March) 1935.

Phrenectomy is a form of collapse therapy and is useful in the treatment of pulmonary tuberculosis.

Operative accidents and complications are encountered less frequently in the child than in the adult. The procedure has great limitations in the infant and is best carried out in the older child past the age of 6 or 8 years.

The authors report fourteen cases in which the operation was successfully performed. In only one case was there complication due to hemorrhage. In practically all the cases, pneumothorax was impractical, owing to adhesions. In seven cases the tuberculous process was in the upper lobe; in two, in the lower lobe, and in three, parahilar. In four of the cases the process was of the ulcerative, fibrotic type with cavitation; in five, of the ulcerative caseous type; in one, of the secondary chronic caseous type; in one, of the extensive ulcerated caseous type, and in one, parahilar.

The operation is particularly indicated in the older child with unilateral localized tuberculosis tending to fibrosis. In the ulcerative caseous type pneumothorax should first be attempted.

Paralysis of the phrenic nerve is brought about by alcoholism or by crushing; the former procedure is not always certain to be successful. A postoperative sanatorium regimen is always indicated and must be rigidly enforced.

SCHLUTZ, Chicago.

Diseases of Blood, Heart and Blood Vessels and Spleen

THE HISTOPATHOLOGY OF THE HEMOPOIETIC TISSUES IN HEMOPHILIA; AN UNEXPLORED FIELD. R. P. CUSTER and E. B. KRUMBHAAR, Am. J. M. Sc. **189**:620 (May) 1935.

Three fatal cases of hemophilia with the observations at autopsy are reported (one patient died of uncomplicated hemorrhage, one of appendicitis and hemorrhage and one of pneumonia). In all the cases the hematopoietic tissues showed normal regenerative ability; in the first two cases the cells were predominantly erythroblastic, and in the third case they were mainly leukoblastic. All three patients showed a marked increase of megakaryoblasts and megakaryocytes in the bone marrow, indicating a relationship of the blood platelets to the hemophilic process.

HENSKE, Omaha.

AN APPARATUS FOR THE THERMAL CONTROL OF SOLUTIONS FOR INTRAVENOUS ADMINISTRATION. J. B. C. ROBINSON and A. S. BARBER, J. Lab. & Clin. Med. **20**:506 (Feb.) 1935.

An apparatus is described which should be useful in maintaining a constant temperature of fluids used intravenously. The apparatus is portable and can be constructed at small cost.

MCMURRAY, Galveston, Texas.

PUNCTURE OF THE INTERNAL JUGULAR VEIN FOR DIAGNOSTIC PURPOSES. JUSTIN J. STEIN, J. Lab. & Clin. Med. **20**:1097 (July) 1935.

Stein describes in detail the technic of puncture of the internal jugular vein. In more than 1,000 cases of puncture there were no ill effects. Diagrams are given which should aid one desiring to use this procedure.

MCMURRAY, Galveston, Texas.

THE CARDIOVASCULAR RENAL DISEASE IN THE NEGRO. JACK C. NORRIS, J. South Carolina M. A. **31**:95 (May) 1935.

Syphilis is the most common cause of cardiovascular disease in the Negro. Forty years was the average age at death in 536 patients who came to autopsy. The condition was more common in the male, owing to hard labor. Substernal pain, dyspnea and edema were the diagnostic cardiac symptoms. Aortic involvement occurred in more than 50 per cent of the patients. Aneurysm was not uncommon, while coronary infection was practically always present. Death was caused by congestive heart failure or pulmonary edema.

WESTON JR., Columbia, S. C.

CARDIAC MENSURATION. FRANKLIN G. WOOD, Lancet **1**:1210 (May 25) 1935.

This study deals with teleroentgenography of the heart in the erect and the prone position. The classic system of measurement was modified, and only three fixed points were used: (1) a point on the right border of the heart, where there is always a distinct notch at the level of origin of the ascending part of the aortic arch; (2) the right cardiophrenic angle, where a small triangle formed by the right dome of the diaphragm, the right auricle and the inferior vena cava is visible; (3) the point at which a line drawn horizontally across from the right cardiophrenic angle cuts the left border of the heart. Lines are drawn between these points to form a triangle, and another line is drawn horizontally across from point 1. This gives four possible measurements, all based on points which can be accurately determined in a good roentgenogram.

These measurements are of little value in themselves unless they can be related in some way to the size of the chest. Relating them to the transverse diameter of the chest was not found sufficiently accurate. In addition to the transverse

diameter of the chest the longitudinal diameter was also measured, and the area of the chest calculated in square centimeters.

A table of average measurements (as noted in 1, 2 and 3) was set up to correspond to the total surface area of the chest. It was found that all the measurements increase uniformly in relation to the surface area of the chest. The diameters are less in the erect than in the prone position.

A study of the outline of the heart and the figures obtained by mensuration enabled the author in many cases to decide from the diagram which valve or valves were diseased.

LANGMANN, New York.

PRIMARY RHEUMATIC CARDITIS. P. HÉRITIER, Arch. de méd. d. enf. **38**:355 (June) 1935.

The case history of a girl of 14 years is reviewed. She had always enjoyed excellent health and had not suffered from chorea or any other manifestation of rheumatism up to the onset of the present attack, which the author interprets as a typical invasion of essential carditis.

On March 22, 1934, there was a sudden rise of temperature, with an elevation to 104 F. in a few hours, as well as a pulse rate of 150 and a feeling of great oppression. Pneumonia was suspected, but auscultation showed no abnormality. The dyspnea increased. During the succeeding days the prostration increased; the pulse rate was scarcely obtainable, and the face deadly pale and covered with a cold sweat. On March 26, after pleuropulmonary explorations had given negative results, a soft, discrete murmur could be elicited over the cardiac area; this was transmitted to the axilla. Gallop rhythm developed. The blood pressure registered 90 mm. systolic and 50 mm. diastolic. The liver and spleen were moderately enlarged, and the abdomen was distended. A striking feature of the syndrome was the total absence of any subjective or objective manifestations of arthritis; pain was not complained of throughout the attack.

As the entire heart seemed involved, a diagnosis of primary carditis was made, and treatment with salicylates was begun immediately, the daily dose amounting to 6 Gm. There was marked amelioration of all the symptoms within twenty-four hours. The cardiac souffle was restricted to the apex but was still transmitted upward and outward. There was oliguria, which was not relieved by the usual management.

A sharp recurrence was experienced on March 31, and during the next four days the patient's condition was extremely critical. Salicylates in doses as large as 8 Gm. daily were administered, and the doses were later increased to 10 and even 12 Gm. Pericarditis now complicated the picture. Orthopnea was continuous; a raucous cough with bloody sputum developed, and fine crepitant râles could be heard over both pulmonary fields. By April 8 the situation became desperate; salicylates were taken poorly, and their use was suspended for twenty-four hours, while insulin with sugar was prescribed, and leeches were placed over the heart. On April 10 a single massive dose of salicylates, to the amount of 10 Gm., was given, and from that moment permanent improvement began. This was hastened by autohemotherapy, the blood being administered intramuscularly in doses of from 8 to 10 cc. Recovery was complete with the exception of a moderate degree of mitral insufficiency.

AMESSE, Denver.

INFLUENCE OF ULTRAVIOLET IRRADIATION ON SOME PHYSICOCHEMICAL CONSTANTS OF THE BLOOD. ANNA SARPERI, Riv. di clin. pediat. **33**:533 (May) 1935.

Observations were made on the blood of rabbits. Irradiation of the animals led to the following reactions: (1) constant but slightly decreased fragility of the red cells, (2) diminution of the sedimentation rate, (3) increased coagulation time, (4) markedly diminished viscosity, (5) increased surface tension and (6) a slight diminution of the alkali reserve.

Prolonged application of the ultraviolet rays to four rabbits always caused a lowering of the red cell count and a loss of weight.

HIGGINS, Boston.

APPEARANCE AND PROPORTION OF SUDANOPHILIC LEUKOCYTES IN INFANTS AND SICK CHILDREN. LEO MOSCHKOWITZ, Jahrb. f. Kinderh. **144**:278 (May) 1935.

Many authors have studied the presence of sudanophilic leukocytes in inflammatory, purulent and toxic conditions.

In the present study the blood was stained with an alcoholic solution of brilliant cresyl blue and sudan III. The former colored the nuclei and granules blue. The fat granules were stained by the sudan III preparation.

Exact determinations were carried out on sixty-one healthy and sick children, with the following findings: Normally, sudanophilic leukocytes are present. The value in the upper range of the normal is about 15 per cent. In normal infants a postprandial or alimentary sudanophilia was demonstrated, which reached its maximum in two hours after meals.

In eleven cases of pneumonia an increase of the sudanophilic cells could be demonstrated. This was likewise true in cases of parapneumonic empyema. After successful operation for this condition the value decreased to normal. There were increased numbers of sudanophilic leukocytes in cases of appendicitis and perityphlitic abscesses. The values returned to normal shortly after operation or drainage of the abscesses.

Two children with meningococcic meningitis showed a distinct increase in the number of sudanophilic leukocytes, in contrast with one child with tuberculous meningitis, in whom they stayed within normal limits.

Several children with eczema, which was classified on the basis of the exudative diathesis, showed a moderate increase in these fat cells, which was explicable on the basis of a disturbance of the fat metabolism accompanying the condition.

An athreptic child with pyloric spasm had an increased value for sudanophilic leukocytes (20 per cent), which was attributed to the increased catabolism leading to enrichment of the blood by fat which was subsequently phagocytized.

A child with severe diabetic coma showed a marked increase in sudanophilic cells. This increase was attributed to the phagocytizing action of the leukocytes accompanying the severe lipemia which was present.

LANDAU, Rochester, N. Y.

LEUCEMIA IN CHILDHOOD. C. DE LANGE, Nederl. tijdschr. v. geneesk. **79**:1677 (April 13) 1935.

This is a clinical lecture on the different types of leukemia observed by the author in seventeen children from 8 months to 10½ years old. The duration of the disease varied between five and one-half weeks and one year. Three other cases in which there was difficulty in making the diagnosis are discussed in more detail.

VAN CREVELD, Amsterdam, Netherlands.

INVESTIGATION OF A NEW BLOOD COAGULANT. B. BRAHN, A. KLARENBEEK and T. LANGNER, Nederl. tijdschr. v. geneesk. **79**:4362 (Sept. 14) 1935.

The authors examined the clotting-promoting effect of a preparation obtained from pectin and consisting nearly exclusively of the oxymethylic ester of galacturonic acid, in rabbits. On oral, intramuscular and subcutaneous administration it was effective three hours after it was given. On intravenous injection it acted immediately, and the effect lasted for many hours; no harm was ever seen even from intravenous injection of doses of 100 cc. of a 2.5 per cent solution.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of Nose, Throat and Ear

THE COMMON COLD: A SURVEY OF RECENT WORK. C. H. BROWNING, Glasgow M. J. **123**:329 (June) 1935.

Colds are the greatest single cause of illness. The duration is from three days to three weeks. Coryza is present in 90 per cent of the cases but occurs alone

in only 18 per cent; cough and sore throat are present in the rest. Sixty per cent of persons have from two to three colds per year; 17 per cent have one or less, and 23 per cent have four or more.

The following theories have been suggested in regard to the causation:

(*a*) The cold is due to some agent not harbored by those attacked in some instances, e. g., Eskimos. (*b*) The agent is probably a filter-passing virus; it can be produced in chimpanzees and cultured in vitro. (*c*) Ordinary organisms found in the nose and throat may play a part in colds; they certainly do in the complications. (*d*) The incidence of colds is independent of climate but has a relation to sudden changes in the weather. (*e*) The incidence of colds has no relation to individual living habits.

In regard to prophylaxis, nasal douches and mouth washes have no effect. Vaccines are apparently of no value. There is no evidence that dietetic factors, except gross lack, play any part. Tonsillectomy and nasal operations have no effect.

In experiments on treatment, a group of university students was divided into two parts. Half were given codeine and papaverine; 75 per cent of these reported improvement in one day. Thirty-five per cent of the controls who thought that they were receiving the same drugs also reported improvement. Acetylsalicylic acid and sodium bicarbonate seemed to have no effect.

SNELLING, Toronto, Canada.

DISCHARGING EARS TREATED BY THE IODINE POWDER METHOD. R. H. BETTINGTON, M. J. Australia **1**:747 (June 15) 1935.

Bettington reports excellent results in the treatment of discharging ears with a powder consisting of iodine (a 0.75 per cent solution) and boric acid (a 99.25 per cent solution). The ear is irrigated and dried and the powder blown in. Both acutely and chronically discharging ears respond well to this method of treatment.

GONCE, Madison, Wis.

CRANIOPHARYNGIOMA (TUMOR OF RATHKE'S POUCH). A. CARRAU and C. M. BARBEROUSSE, Arch. de méd. d. enf. **38**:261 (May) 1935.

Among the cerebral tumors, the suprasellar growths or craniopharyngiomas, occupying the pharyngohypophyseal canal, are readily detected by their characteristic features. These neoplasms are always congenital and are commonly situated above the sella turcica; they may even be intrasellar and in any event are visible, in suitable roentgenograms, in 85 per cent of the cases.

The diagnosis rests chiefly on a clinical syndrome of surprising constancy:

1. Endocrine lesions, infantilism, arrest of growth, diabetes insipidus, obesity, hypogenitalism, etc.

2. Atrophy of the optic nerves accompanied by other ocular lesions, such as bitemporal hemianopia.

3. Calcifications above the sella turcica, with normal integrity of that structure.

The symptomatology varies with the age of the patient, the size of the tumor and its evolution. The authors report a case in a girl of 11 years, supplemented with complete clinical notes, roentgenograms and a résumé of the observations at autopsy.

AMESSE, Denver.

MUCOCUTANEOUS ULCERATIVE TUBERCULOSIS OF THE NOSE, PHARYNX AND EYES. M. GRENET, P. ISAAC-GEORGES and L. LANGLOIS, Bull. Soc. de pédiat. de Paris **32**:97 (Feb.) 1934.

A girl, 3 years old, had an ulcerative lesion on the lower outer margin of the right side of the nose at the age of 1 year. This was accompanied by coryza, which persisted for many months. The eyes became involved with phlyctenular keratoconjunctivitis, and indolent ulcerative lesions appeared on the soft palate

and pharynx. The patient presented the appearance of a scrofulous child. The tuberculin reaction was strongly positive, and a roentgenogram of the chest showed evidence of tuberculous infection. The Wassermann reaction of the blood was negative. Although the occurrence of a tuberculous infection of the scrofulous type has been described as developing on a syphilitic background, one should bear in mind that it may exist in the absence of syphilis.

BENJAMIN, Montreal, Canada.

DISORDERS OF SPEECH. SUZANNE BOREL-MAISONNY, Rev. franç. de puériculture **2**:279 (Nov.) 1934.

The complexity of the study of disorders of speech is due in part to the fact that while the same causes always produce the same effects, similar effects may be engendered by very diverse causes. Pathologic sounds, such as those due to laryngospasm, hoarse breathing and nasal twang, are found in children with paralysis of the soft palate, in children with adenoids, the high arched palate typical of the mongolian idiot or cleft palate. Spasmodic disorders are found in stammerers, persons with epilepsy, mongolian idiots and subjects suffering from meningeal irritation or the sequelae of encephalitis. Delayed speech, with baby talk and voice, is seen in normal children as well as in mentally deficient children.

CRANE, Chicago.

CHRONIC TONSILLITIS. W. SCHÜTZ, Arch. f. Ohren-, Nasen- u. Kehlkopfh. **139**: 198 (March 20) 1935.

Schütz points out that the clinical connection of recurrent tonsillitis with articular, renal and cardiac disturbances led to a search for the morphologic forms of chronic tonsillitis. After mentioning other authors who have investigated this problem, he reports histologic studies of the palatine tonsils obtained by operation from patients with chronic tonsillitis. He differentiates two types of tonsillitis: the chronic hypertrophic form and the chronic atrophic form. He concedes that a strict differentiation between these is not always possible, for there are transitional forms. In comparing the histologic with the clinical aspects he found that in chronic hypertrophic tonsillitis the tendency toward complications is considerably less than in the chronic atrophic form. In elucidating his conception of complications he points out that the clinical aspects of chronic tonsillitis are determined by the always existing suppuration of the palatine tonsils, which at certain intervals flares up in acute inflammation. Complications may be of two types: On the one hand, the continuous spreading may result in chronic peritonsillitis or in peritonsillar abscess; on the other hand, the inflammatory complication may spread by way of the lymph or blood channels. Schütz disregards the severest forms of the metastatic type of complication, such as sepsis, thrombosis of the jugular vein, abscesses of the cervical lymph nodes and so on, and gives his attention only to articular and muscular rheumatism, cardiac defects and renal disease, in which a blood-borne infection must be assumed. It is a well known fact that severely fissured small tonsils cause peritonsillar abscess and articular rheumatism more often than do other kinds. The author's observations reaffirm this fact. Of 100 pairs of tonsils examined, 68 were of the chronic hypertrophic type and 32 of the chronic atrophic type. Of the patients with hypertrophic tonsils, 45.6 per cent presented complications; of those with atrophic tonsils, 72 per cent. Schütz points out further that in the majority of patients with chronically hypertrophic palatine tonsils the pharyngeal tonsils are likewise enlarged, whereas in patients with chronically atrophic tonsils there are usually no pharyngeal tonsils. He thinks that the age and the constitution of the patient are likewise decisive in the development of atrophic or hypertrophic tonsillitis. The hypertrophic form usually predominates in younger patients; the atrophic one, in older patients. The author shows that this knowledge is helpful in the treatment of chronic tonsillitis.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

TOXEMIA TONSILLOPULMONALIS FULMINANS INFANTUM. LORENTZ HEERUP, Hospitalstid. **78**:169 (Feb. 12) 1935.

By this name the author designates a violently acute infection that is frequently fatal within twenty-four hours, which may be sporadic or nosocomial in poorly nourished children under 18 months old who often have had various catarrhal infections. Clinically, there are symptoms of septic hyperpyrexia without apparent focal involvement. On examination mild tonsillopharyngitis and obstructive hyperemic edematous pulmonary affection are found. Microscopically, a massive growth of staphylococci, streptococci and pneumococci appears in the tonsils and lungs and frequently extends to the gastro-intestinal tract, but the blood and remaining organs are sterile. A theoretical explanation may be found in transmission from infant to infant, with increased virulence of the microbes, or in sensitization producing the pulmonary edema, with diffuse spreading of the microbes, just as in experiments with animals with pneumococci, and active absorption of the toxin in the tonsils and lungs.

VINTON, Brooklyn.

Diseases of Lungs, Pleura and Mediastinum

LIPOID PNEUMONIA IN CHILDREN. HARVEY F. GARRISON, South. M. J. **28**:322 (April) 1935.

Garrison believes that it is evident that pulmonary inflammations due to the aspiration of lipoids are not detected often enough clinically. This is mainly because the initial lesion in the lungs is not sufficiently widespread to show any characteristic clinical or roentgenologic signs. In the great majority, in fact, in practically all the cases reported, the condition has been diagnosed post mortem.

Garrison suggests that a diagnosis can be made if there is a history of the administration of an oily substance via the nasopharynx or orally over a long period, which, if followed by hacking cough, rapid respirations without dyspnea and atypical pulmonary consolidation, which is in the central posterior region and mostly on the right, in a debilitated infant, should make one suspect lipoid pneumonia. Tuberculosis, of course, must be ruled out. The finding of mononuclear cells containing lipoid substances in expectorated material has been suggested as evidence of this disease but has not conclusively been proved to be of diagnostic value.

The present study indicates the need for conservatism in the treatment of children by means of oily substances administered via the nasopharynx, as well as orally. The author has discontinued the use of liquid petrolatum as a cathartic and the use of oil drops of a similar nature in the nose in small undernourished infants. When cod liver oil is poorly taken it seems best to give one of the more concentrated preparations, even though the antirachitic potency is probably not as high. In the light of the present findings relative to the use of lipoid substances, it would seem to be the best policy to sound a note of warning and to advise the necessary precautions as to their general use.

SCHLUTZ, Chicago.

ATELECTATIC OR COMPENSATORY BRONCHIECTASIS. L. FINDLAY, Arch. Dis. Childhood **10**:61 (April) 1935.

The view that the bronchiectasis accompanying pulmonary collapse is compensatory in nature is supported. The specific cause is the inability of the lung to fill the thoracic cavity and hence the necessity for some space communicating with the external air (alveolus or bronchus) to dilate.

The significance in the roentgenogram of the so-called triangular shadow occupying one or the other diaphragmaticovertebral angle is discussed. This shadow is shown to be caused by encysted effusions, fibrosis of the lung and

thickened pleura, pneumonic consolidation and collapse of the lung. Stress is laid on the reinflatability of the lung as essential for a diagnosis of pulmonary collapse.

Some previously recorded cases of atelectatic bronchiectasis are considered, and the correctness of the diagnosis is submitted to criticism.

Three cases of bronchiectasis with an accompanying triangular shadow are described. In all the cases the bronchiectatic lesion was situated at the base of the right lung and was of mild degree, and there was complete recovery. In one case the shadow was certainly due to collapse of the lung, and it is concluded that this was the cause of the bronchiectasis. In another case collapse was the probable cause, and in the third case pneumonic consolidation appeared to be the more likely etiologic factor.

KELLY, Milwaukee.

ATELECTATIC BRONCHIECTASIS. REGINALD LIGHTWOOD, Proc. Roy. Soc. Med. **28**:1192 (July) 1935.

A girl, aged 6 years, had a history of many attacks of pneumonia since birth, and she had an almost constant cough. In August 1933, signs of pneumonia were present at the bases of both lungs, and the child was discharged to a home for convalescents with some signs still persisting. In October 1933, she was readmitted to the hospital, again with signs of pneumonia at the base of the left lung. Roentgen examination following the injection of iodized poppy-seed oil 40 per cent showed collapse of the lower lobe of the left lung, with bronchiectasis in the atelectatic lung. In December 1934, the child was admitted to the hospital a third time with signs of pneumonia at the base of the left lung. The question of lobectomy was considered.

WILLIAMSON, New Orleans.

CAPILLARY BRONCHITIS AND ITS TREATMENT BY BLOOD TRANSFUSION. B. TASSOVATZ, J. de méd. de Paris **55**:396 (May 2) 1935.

Two infants with capillary bronchitis, 3 and 4 months old, respectively, were treated by the transfusion of 80 cc. of citrated blood introduced into the superior longitudinal sinus after the removal of a similar amount. Marked improvement occurred from twelve to fifteen hours after the transfusions, and both infants recovered.

LESLIE, Evanston, Ill.

THE TRIANGULAR IMAGES AT THE BASE OF THE THORAX. R. DEBRÉ and M. LAMY, J. de méd. de Paris **55**:737 (Aug. 22) 1935.

The authors discuss the difficulties of interpreting triangular shadows at the base of the lung. For many years a right-angle triangular shadow with the short side at the diaphragm and the hypotenuse crossing the pulmonary field to the hilus was interpreted as being due to mediastinal pleurisy. The authors had observed such shadows in many cases of bronchiectasis and were dissatisfied with the interpretation just given. They believe that a more correct view was held by Anspach and others, who regarded such shadows as due to atelectasis following stenosis of a bronchus. They call attention to the existence of similar shadows in whooping cough and state the belief that the lesions of the mucosa are sufficient to produce plugging of the bronchioles, resulting in regions of atelectases. Complete closure of a bronchus by tuberculous lymph nodes may lead to similar pictures. In small infants displacement of the mediastinum may also result.

LESLIE, Evanston, Ill.

CLINICAL SYNDROME AND PARENCHYMAL ALTERATIONS OF THE LUNGS IN BRONCHOPNEUMONIA OF INFANCY. F. PONTIERI, Pediatria **43**:489 (May) 1935.

A comparative study of the clinical course and observations at autopsy in sixty cases of bronchopneumonia in children between the ages of 2 days and 24 months is reported. Pontieri found that alterations of the bronchial, parenchymal

and hilar tissues differed in extent and degree in direct relation to the severity of the clinical syndrome.

Histologic examinations frequently revealed descending bronchial lesions, while the blood vessels, though always participating in the pathologic processes, rarely exhibited organic changes.

SIGNORELLI, New Orleans.

ELECTROCARDIOGRAPHIC STUDIES OF PATIENTS WITH PROGRESSIVE MUSCULAR DYSTROPHY. S. MOSCHINI, Riv. di clin. pediat. **33**:429 (April) 1935.

The possibility that myocardial changes may accompany the changes in the skeletal muscles in patients with progressive muscular dystrophy led Moschini to study the electrocardiograms of six children (from 4 to 13 years old) with progressive muscular dystrophy. In each case there was an accentuation of the Q wave in the second and third leads.

HIGGINS, Boston.

A NEW USE FOR EMETINE IN PARASITOLOGY. PEDRO KOURÍ, JOSÉ G. BASNUEVO and ROGELIO ARENAS, Arch. de med. inf. **4**:21 (Jan.-March) 1935.

The authors have used emetine hydrochloride in doses of 0.5 cg. per kilogram of body weight with complete success in six cases of distomiasis due to Fasciola hepatica. They wish to emphasize the fact that emetine is a specific for this type of parasite, as they have thoroughly checked the microscopic changes of the parasite's ovas found in the bile obtained by serial duodenal intubations.

SANFORD, Chicago.

TREATMENT OF BRONCHOPNEUMONIA BY FIXED ABSCESSES. ATHAYDE FONSECA, Arch. de pediat., Rio de Janeiro **7**:244 (Feb.) 1935.

The author describes three cases of bronchopneumonia in which the patients showed no improvement after classic treatment but responded immediately after abscesses had formed following the injection of from 1 to 2 cc. of essence of turpentine.

SANFORD, Chicago.

TWO CASES OF PNEUMOTHORAX IN INFANTS. C. PELFORT and MARIA ISABEL CRUZ, Arch. de pediat. d. Uruguay **6**:99 (March) 1935.

The authors report two cases of this complication in two infants, one 9 months old, the other, 20 months old.

In the younger infant a pulmonary tuberculous process was responsible. In the older infant the condition was a sequel to an acute bronchopulmonary process. The process terminated fatally in the younger infant.

SCHLUTZ, Chicago.

ATELECTASIS AS A CAUSE OF BRONCHIECTASIS IN CHILDREN. LOLAR VILAR and ERNESTO ALONSO, Crón. méd., Valencia **39**:188 (March 15) 1935.

The authors believe that atelectasis is frequently a cause of bronchiectasis in children and give the histories of fourteen patients, with twenty-two illustrative roentgenograms, to show this. Physiologic atelectasis may be prevented in the first days of life by encouraging vigorous respiratory movements in the new-born. The inferior lobe of the lung is easily compressed and is the lobe that is most usually effected. The condition can be diagnosed by a triangular shadow at the base.

SANFORD, Chicago.

TOXIC EFFECT OF FOUL-SMELLING PUS IN PLEURAL EMPYEMA. E. SCHNEIDER, Deutsche Ztschr. f. Chir. **24**:521, 1935.

It is a clinical observation that the more foul-smelling the pus in empyema the greater is the toxic effect on the patient. The odor does not appear to be

associated with any particular bacterial flora, and when free drainage is secured the odor tends to disappear, though the bacterial flora may not be altered. The author found that the foul-smelling principle of the pus could be completely extracted with ether. When this extract was compared with the extract of pus without a foul odor it was found that the extract of the foul-smelling pus possessed a much higher bromine number. Sulfur could not be demonstrated in the extract, hence mercaptan could be ruled out as the source of the odor. Tryptophan and skatole do not bind bromine; hence these substances may also be excluded. Schneider attributes the foul odor to the presence of acrolein and allylamine. These compounds produce a toxic effect in pleural empyema with foul-smelling pus in addition to the effect of the bacterial toxins. GLASER, Rochester, N. Y.

SOME LESS COMMON LUNG COMPLICATIONS IN ASTHMATIC CONDITIONS IN CHILDREN. B. SÖDERLING, Acta pædiat. **17**:528, 1935.

Söderling emphasizes the difficulties which are sometimes encountered in making an early diagnosis of asthma in children, particularly when the initial symptomatology is atypical, incomplete or nonspecific. He draws attention to some uncommon, and hence doubly confusing, complications, such as recurrent, localized atelectasis, bronchiectasis, and pleural shadows revealed by roentgenogram which may simulate the characters of tuberculosis. There are twenty-four excellent reproductions of roentgenograms. MCCUNE, New York.

PULMONARY COLLAPSE IN CHILDREN. M. DE BRUIN, Nederl. tijdschr. v. geneesk. **79**:2902 (June 15) 1935.

De Bruin describes various forms of pulmonary collapse with different etiology in children. The signs presented on clinical and roentgen examination which enable one to diagnose this condition with more or less accuracy are mentioned. An attempt to clear the obstructed bronchus by means of the bronchoscope should be made as soon as possible after the onset of the collapse because of the danger of the development of bronchiectasis.

VAN CREVELD, Amsterdam, Netherlands.

BROADENING OF THE UPPER PART OF THE MEDIASTINAL SHADOW IN SMALL CHILDREN AND ITS DIAGNOSTIC SIGNIFICANCE IN MEDIASTINAL PLEURISY. H. E. A. FERMIN, Nederl. tijdschr. v. geneesk. **79**:3059 (June 22) 1935.

After observing three cases the author discusses the difficulties which may arise in roentgen examination of the upper part of the mediastinum in small children. Special attention is drawn to the occurrence of pleuritis mediastinalis superior, which gives a roentgen picture showing great resemblance to that of hyperplasia of the thymus. VAN CREVELD, Amsterdam, Netherlands.

Diseases of the Gastro-Intestinal Tract, Liver and Peritoneum

TRAUMATIC DUODENAL ULCER IN A TEN YEAR OLD BOY. JACK WITHERSPOON, Am. J. Digest. Dis. & Nutrition **2**:135 (April) 1935.

A case of duodenal ulcer with a typical history and roentgen deformity is reported. The condition followed a fall on the abdomen. The symptoms were noted within twelve hours after the injury. MORRISON, Savannah, Ga.

CHOLEDOCHUS CYST WITH A DOUBLE COMMON BILE DUCT. WILLIAM B. SWARTLEY and S. DANA WEEDER, Ann. Surg. **101**:912 (March) 1935.

Swartley and Weeder believe this to be the only case reported of choledochus cyst with a double common bile duct. Cases of both conditions occurring alone have been reported.

The symptomatology of double duct is not characteristic. The patient is usually free from symptoms until obstruction of the patulous duct occurs, in which case indigestion, pain or jaundice with localized tenderness lead the observer to make a diagnosis of disease of the biliary tract.

In cases of choledochus cyst, pain and jaundice occurring intermittently and the presence of a tumor mass in the upper part of the abdomen are the common findings.

The case reported was that of a 4 year old boy. The chief disorders were nausea and abdominal pain. There were moderate abdominal distention and definite tenderness in the epigastrium. No mass could be palpated. Peristaltic waves were present. The temperature was 100 F. The pulse rate was from 96 to 120. White blood cells numbered 14,600, with 70 per cent neutrophils, 27 per cent lymphocytes and 3 per cent mononuclears. The diagnosis was made at operation. The operative procedure is given in detail.

BANTIN, Omaha.

MECKEL'S DIVERTICULUM. CHARLES E. FARR and MADELINE PENKE, Ann. Surg. **101**:1026 (April) 1935.

Meckel's diverticulum is the most frequent congenital anomaly of the intestinal tract, being noted in approximately 2 per cent of persons at autopsy. It is apparently present more often in males than females, occurring in the ratio of 3:1. In a considerable number of cases it causes active symptoms and threatens life.

Intestinal bleeding seems characteristic of the condition. This is accompanied by increasing anemia, with symptoms of perforation later, owing to the development of an ulcer in the diverticulum at the edge of an island of heterotopic gastric mucosa. The incidence of gastric mucosa in Meckel's diverticulum is difficult to estimate.

In children the condition must be differentiated from intussusception, hemorrhagic disease of the new-born, hemophilia and purpura.

Excision of the diverticulum is the usual and proper treatment.

BANTIN, Omaha.

FIVE HUNDRED FOREIGN BODIES IN THE STOMACH. R. STEWART KENNEDY, Brit. M. J. **1**:1262 (June 22) 1935.

Operation was performed on a man, 28 years of age, who had a mental disorder, with abdominal symptoms, and foreign bodies were removed from the stomach. The patient died. The number and variety of articles found in the stomach are almost unbelievable.

ROYSTER, University, Va.

SUMMER DIARRHEA AND ACUTE INTUSSUSCEPTION. P. N. RAY, Indian J. Pediat. **2**:227 (July) 1935.

In a brief discussion of intussusception Ray records three cases of acute intussusception complicating summer diarrhea in children. Two of the patients were nearly 3 years of age. In each case the intussusception was of the ileocecal variety. Peyer's patches in the distal part were edematous and enlarged, and the mesenteric and ileocecal lymph glands were enlarged.

GONCE, Madison, Wis.

GLYCOGEN ACCUMULATION DISEASE. P. M. ANDERSON, M. J. Australia **1**:362 (March 23) 1935.

Anderson describes the recent progress in two cases of glycogen accumulation disease. Tests done in these two cases led her to agree with van Creveld's conclusion that the mechanism of the accumulation is due to some inherent quality in the glycogen built in the liver rather than to any lack of enzymes to split it down to dextrose. The carbohydrate metabolism in general and the significant facts involved in the production of von Gierke's disease are briefly discussed.

GONCE, Madison, Wis.

HELMINTHIASIS OF THE CHILD AND ITS TREATMENT. ROUÈCHE and J. TERRASSE, J. de méd. de Paris **55**:205 (March 7) 1935.

The authors give an excellent review of the recognition and treatment of intestinal parasites in the child after classifying these according to morphology. They discuss the incidence and manifestations of infection, the recognition of parasites in the stools and the treatment of the various types of helminthiasis. Numerous formulas and specific instructions are given.

LESLIE, Evanston, Ill.

A CASE OF PRIMARY CANCER OF THE LIVER IN A CHILD FOURTEEN MONTHS OF AGE. PÉCLARD, J. de méd. de Paris **55**:578 (June 27) 1935.

The child in question was in excellent health until a month before admission to the hospital. During that time he had some diarrhea, perspired a great deal, slept poorly and lost weight. The liver extended below the umbilicus. There was no anemia. Death occurred ten days after admission, probably precipitated by hemorrhage from one of the cancerous areas into the peritoneum. Histologic examination of the liver showed large areas of neoplastic epithelial cells, some of which were filled with fat. Necrosis was marked in some areas. The whole tumor was traversed by bands of fibrous tissue.

LESLIE, Evanston, Ill.

REACTION OF STOOLS IN INFANCY. R. PACHIOLI and V. MENGOLI, Pediatria **43**:617 (June) 1935.

The various methods of determining the reaction of stools is fully discussed, and the colorimetric method used by the authors is described. A review of the literature concerning the reactions of stools in adults and in breast-fed and artificially fed infants is presented, together with the authors' findings in their examination of stools from three hundred and sixty-six children under 2 years of age and fifteen children over 2 years of age.

Their observations indicate that the normal reaction of stools of breast-fed infants is acid (average p_H, 5.6), while the normal reaction of stools of artificially fed children is alkaline, with variations according to the types of food ingested. The stools of children over 2 years of age are acid and generally are not influenced by the type of food ingested.

SIGNORELLI, New Orleans.

TREATMENT OF ALIMENTARY INTOXICATION WITH THE INTRAVENOUS DROP METHOD. IRMGARD GRUBE, Monatschr. f. Kinderh. **61**:439, 1935.

Grube tried the method of prolonged drop infusions in the cases of sixteen toxic infants aged from 3 weeks to 11 months. In the first group of seven, the intoxication was complicated by infection. In these, a 12 to 25 per cent solution of dextrose was used in either plasma or Ringer's solution. In the second group of nine cases of uncomplicated alimentary intoxication, the author used a 5 per cent solution of dextrose; the amount of fluid was estimated according to the method reported by Karelitz and Schick.

The results were unsatisfactory in all the cases. Only three of the sixteen infants survived.

GERSTLEY, Chicago.

TREATMENT OF CHRONIC APHTHOUS STOMATITIS. O. FRIED, München. med. Wchnschr. **82**:706 (May 2) 1935.

For the treatment of chronic aphthous stomatitis Fried advises brushing the teeth and rinsing the mouth with soap. The author had the condition himself and after trying all forms of therapy found soap the only efficacious one.

BRAHDY, Mount Vernon, N. Y.

APPENDICITIS AND PERITONITIS. EDMUND NOBEL, Wien. klin. Wchnschr. **48**:596 (May 10) 1935.

Nobel notes that the classic symptoms of appendicitis are well known, being chiefly vomiting and pain in the region of the appendix or over a larger area. In nonacute appendicitis vomiting occurs only once or twice, and there is some pain on pressure in the ileocecal region. There may be a slight fever or no rise in the temperature. In severe forms of appendicitis vomiting and pain are more marked, and there is usually an irregular fever. The pulse rate may be from 110 to 150. Appendicitis associated with general peritonitis usually ends fatally in from three to six days. There are signs of general sepsis, cyanosis, cold hands, apathy and a rapid pulse rate. In appendicitis vomiting is an especially important sign. At the beginning it is found in more than two thirds of the cases. It is especially noteworthy in cases in which there are no faults in the diet and no constipation. On the first day there may be diarrhea, which is followed by constipation. Often there is retention of urine, loss of appetite, sleeplessness and anxious restlessness. Among the conditions which may be confused with appendicitis are the following: pneumococcic peritonitis, invagination of the intestine, body pains in infectious diseases, acetonemic vomiting, navel colic and hysteria.

ABT, Chicago.

PRIMARY CARCINOMA OF THE LIVER. ERNST GJØRUP, Hospitalstid. **78**:211 (Feb. 19) 1935.

The author describes in detail the clinical and operative findings in a case of carcinoma of the liver in a boy 13 years of age. Biopsy and postmortem examination proved this condition to be a primary malignant growth of the liver.

ELGHAMMER, Chicago.

SPECIFIC ANTISUBSTANCES IN URINE IN WEIL'S DISEASE. J. VAN DER HOEDEN, Nederl. tijdschr. v. geneesk. **79**:1943 (April 27) 1935.

In 17 of 18 subjects suffering from Weil's disease the urine was found to contain agglutinins (and lysins) for Leptospira icterohaemorrhagiae or Leptospira canicola in titers up to 250. In 33 of 35 subjects who had recovered from Weil's disease the urine as well contained the agglutinins (the reaction was negative in one subject after sixteen months and in another after two years). The agglutination occurred a few days later in the urine than in the blood serum. It was found in the urine on the eighth day of the illness and persisted there much longer than in the cerebrospinal fluid. No relation was found between agglutination in the urine and albuminuria or between agglutination and signs of a renal lesion.

Among 146 controls (37 of whom had albuminuria and 5 infective jaundice) the urine showed a completely negative reaction in 143; 2 showed a dubious reaction with a dilution of 1:2, and 1 showed a distinct reaction with this dilution. Ten dogs clinically ill from Weil's disease and 5 animals suspected of having this disease, all had agglutinins (lysins) in the urine (in titers up to 2,000). In dogs the agglutinins in the urine also appeared later than in the blood serum. Of 11 wild rats, 6 showed agglutinins in the blood, and 4 of these showed agglutinins in the urine also.

VAN CREVELD, Amsterdam, Netherlands.

Nervous Diseases

CHEMICAL STUDIES IN THE EPILEPTIC SYNDROME: II. NOCTURNAL AND DIURNAL RHYTHM IN BLOOD CHEMISTRY. HELEN HOPKINS, Am. J. Psychiat. **92**:75 (July) 1935.

The physiology and chemistry of sleep are discussed. The results of studies previously reported point to the chemical condition in the nocturnal period, or

period of sleep, as having unusual significance in the syndrome of epilepsy with a predominance of seizures. This paper deals with serial chemical determinations of blood throughout a twenty-four hour period for each of five normal persons and seven subjects with epilepsy. These determinations were confined to the elements which are recognized to be related to the convulsive state: plasma p_H; carbon dioxide combining power; amount of serum calcium, total and diffusible; the albumin, globulin and inorganic phosphorus contents of the serum, and the hemoglobin concentration.

The results indicate that, whereas for the normal group the variation in the plasma p_H was negligible, for the group with epilepsy a higher level of p_H (around 7.5) was shown. There was little variation from hour to hour. The carbon dioxide combining power of the plasma declined slightly during the nocturnal period. The same may be stated for the diffusible and total calcium contents of the blood. The most pronounced chemical change of the blood before convulsion was an elevation in the inorganic phosphorus level (precipitation of calcium and thus an increase in cellular irritability). The highest values for inorganic phosphorus coincided with the maximum hemodilution. The serum albumin and globulin values declined between the hours of 9 p. m. and 3 a. m.

The changes in the acid-base balance, water-shifting and p_H of the blood are of the type to encourage the occurrence of the seizures in the latter half of the period of sleep.

JAHR, Omaha.

THE MECHANICAL MANAGEMENT OF BRAIN ABSCESS. A. W. ADSON and W. M. CRAIG, Ann. Surg. **101**:7 (Jan.) 1935.

Adson and Craig review ninety-seven cases of abscess of the brain. Cases of epidural abscess were excluded. Sixty of the patients were male and thirty-seven female. The average age was 24 years. Three patients were less than 3 months of age. In forty cases the abscess was situated in the frontal lobe, in thirty-six in the temporosphenoid area, in two in the occipital area and in thirteen in the cerebellar area. In the remaining six cases the abscesses were distributed in other scattered areas. The invading organisms were Staphylococcus albus or Staphylococcus aureus in nineteen cases and Streptococcus haemolyticus in eleven cases. Headache was present in seventy-nine cases; nausea and vomiting, in sixty-one; choked disk, in forty-nine and blindness in ten. Fifteen patients had preoperative jacksonian convulsions, and twenty had grand mal seizures. The neurologic symptoms varied according to the size and the position of the abscess. The degree of recovery was in relation to the injury done by inflammation and surgical manipulation.

With regard to mortality, the results improved with the experience of the surgeon. The mortality rate dropped as soon as the surgeon delayed drainage until encapsulation took place. In cases of abscess of the temporosphenoid lobes there was a lower mortality rate when drainage was established through a clean field in the temporal area than when it was carried out through a suppurating mastoid incision. The sealing of the meninges and cortex about the drainage tract to prevent contamination has improved convalescence and lowered the mortality rate. Adequate continuous drainage with gauze packs and rubber tube drains has prevented recurrent abscess and cerebral herniation. By these means, in fourteen of fifteen consecutive cases of abscess situated above the tentorium and in two of three cases of cerebellar abscess, recovery occurred.

Adson and Craig think that it is well to administer supportive treatment during the initial stage of infection and to delay drainage until clinical signs indicate that immunity has been established. They also prefer the institution of adequate continuous drainage through a surgically sealed wound to the various conservative or ultraradical measures employed.

GRANT, Philadelphia. [ARCH. NEUROL. & PSYCHIAT.]

EFFECTS OF ALTERATIONS IN POSTURE ON THE CEREBROSPINAL FLUID PRESSURE. JULIUS LOMAN, ABRAHAM MYERSON and DAVID GOLDMAN, Arch. Neurol. & Psychiat. **33**:1279 (June) 1935.

The authors measured the spinal fluid pressure to determine variations which occur with alterations in posture. The individual conclusions are too long for summary.

The observations made on the cerebrospinal fluid pressure indicate that, although the pressure receives its initial force from the capillaries of the choroid plexus, it is modified by a constantly shifting set of factors, the essential one being the venous pressure. In view of the extremely elastic venous wall which separates the cerebrospinal fluid from the thoracic, abdominal and external pressure, it seems inappropriate to refer to the intracraniovertebral cavity as a closed box or semi-rigid container.

BEVERLY, Chicago.

MICROCEPHALIA VERA. J. GODWIN GREENFIELD and JULIAN M. WOLFSOHN, Arch. Neurol. & Psychiat. **33**:1296 (June) 1935.

After a comprehensive review of the literature and microscopic study of two cases of microcephalia vera, the authors conclude that the underlying pathologic processes are at work before the fourth month of fetal life. Also it is evident that not one but many diverse factors can affect the germ cell or the young embryo and produce the condition.

BEVERLY, Chicago.

TUMORS IN THE SPINAL CANAL IN CHILDHOOD: AN ANALYSIS OF THE LITERATURE WITH REPORT OF A CASE. WALLACE B. HAMBY, J. Nerv. & Ment. Dis. **81**:24 (Jan.) 1935.

A white girl at the age of 6 years was tossed over her father's back during play. That night she awakened with pain in the lumbar region. Thereafter the pains appeared frequently, especially in the popliteal region on the left and in the back. During the year after the injury a lump appeared in the dorsolumbar region and the patient became stooped. Weakness developed in the legs until the child, who was 10 years old at the time of writing, was unable to support herself. At the age of 8 or 9, paresis of the left ankle developed. Except for measles and an occasional cold, the past history revealed nothing abnormal. Physical examination showed marked emaciation, though the patient was not acutely ill. The thyroid gland was profusely enlarged; the abdomen was tense, with a distended bladder extending to the level of the umbilicus. The anal sphincter was relaxed, and the mucosa moderately prolapsed. The spine was distorted due to scoliosis of the lumbar region to the left, kyphosis from the tenth dorsal to the third lumbar vertebra, with marked protrusion of the spinous processes of the first, second and third lumbar vertebrae and lordosis from the fourth lumbar vertebra to the sacrum. The knee jerk and achilles reflex were absent on both sides. Hyperesthesia was present over the gibbus from the twelfth dorsal to the fourth lumbar vertebra, and saddle anesthesia and hypesthesia were noted over the region from the first lumbar to the fifth sacral vertebra. The ventral flexors of the trunk were very weak, as were the muscles of the lower extremities. Lumbar puncture yielded a little blood but no fluid. Tissue aspirated from the subdural space resembled ependymoma microscopically.

The diagnosis was tumor of the spinal cord dilating the vertebral canal. Treatment consisted of excision followed by five irradiations of 275 roentgens each. Improvement was gradual.

A comprehensive review of the literature on intraspinal tumors in childhood is included.

JAHR, Omaha.

SPECIFICITY OF STREPTOCOCCI ISOLATED IN STUDIES OF DISEASES OF THE NERVOUS SYSTEM: EXPERIMENTAL REPRODUCTION OF PERSISTENT SNEEZING AND CONVULSIONS. EDWARD C. ROSENOW, J. Nerv. & Ment. Dis. **81**:138 (Feb.) 1935.

CASE 1.—A schoolgirl, aged 16, suffered from persistent sneezing varying in intensity but lasting during most of the time for eight days. There were also marked disturbances in the rate and amplitude of respiration. Periods of hyperpnea and great restlessness alternated with apnea, holding the breath, exhaustion, drowsiness and lethargy. The spinal fluid was normal. The temperature was normal or slightly elevated. Improvement followed the first injection of concentrated encephalitis antistreptococcus serum. The sneezing disappeared completely in thirty-six hours after several additional injections of serum of 10 cc. each.

CASE 2.—A man, aged 29, suffered from postinfluenzal epileptiform convulsions. The patient had been in bed with influenza for three days and, except for a persistent cough, seemed fully recovered. Ten days later he was seized with a generalized convulsion of about eight minutes' duration.

Cultures of streptococci isolated from the nasopharynx of the two patients when injected into rabbits produced sneezing and convulsions, respectively. The technic is described fully, and photomicrographs of the brains of the animal studied are submitted.

JAHR, Omaha.

THE TREATMENT OF ENURESIS IN CHILDHOOD. AIMS C. MCGUINNESS, M. Clin. North America **19**:286 (July) 1935.

Enuresis may be defined as functional incontinence of urine, nocturnal, diurnal or both, in children of 3 years of age or over. While a physical cause should always be sought by careful physical and urologic examination, a psychogenic basis may be found on careful analysis in a majority of cases.

Enuresis is often but one of many difficulties presented by the child, who may also exhibit such disturbances in behavior as tantrums, anorexia, negativism, etc. The act may be aggressive or, more often, submissive. A child may voice his protests against dominance by adults through the exercise of his function of elimination, of which he is sole master. He may resent the responsibilities incident to increasing age and express his feelings by infantile acts. Or it may be that the bed-wetting is but reaching out for attention, which he feels he has lost.

Successful treatment must take these and many other factors into account and must be directed toward the adjustment of the child to his environment. The methods by which this may best be accomplished vary with the child, but they must include establishing friendly relations with the child, gaining his confidence and interest and helping him to develop new channels of activity and self-expression. Also, the parental attitude toward the child and his weakness must be clarified, an important and often a difficult undertaking.

EUGENE SMITH, Ogden, Utah.

BENIGN LYMPHOCYTIC CHORIOMENINGITIS (ACUTE ASEPTIC MENINGITIS). CHARLES ARMSTRONG and PAUL F. DICKENS, Pub. Health Rep. **50**:831 (June 21) 1935.

A symptom complex of headache, fever, irritation of the meninges and increase in the pressure of the cerebrospinal fluid and in the number of cells to over 50 (with lymphocytes predominating), in association with normal chloride, sugar and urea contents and a negative Wassermann reaction of the spinal fluid, is a clinical entity, which has been previously designated in man as acute aseptic meningitis. The virus of Armstrong produces a symptom complex in monkeys similar to that just described, while, conversely, the blood serum of patients who have recovered from the disease protects animals from the virus of Armstrong. This disease occurs sporadically in man and has been transferred experimentally to animals. Traub has isolated a virus from white mice and Rivers and Scott

have isolated a virus from human patients, which are serologically identical with the strains of the Armstrong virus kept at the National Institute of Health. The cases reported in this paper were distributed over scattered geographic areas and had their origin in California, Maryland, the District of Columbia, Illinois, Ohio and Virginia.

The symptom complex is a disease entity, and, while on the basis of priority the condition should be designated "acute aseptic meningitis," in view of the recent advance in the knowledge of its etiology, the authors suggest the term "acute lymphocytic choriomeningitis" as a more accurate designation. The etiologic agent is a filtrable virus, first described by Armstrong and Lillie. Monkeys, mice and guinea-pigs are susceptible to the virus, and it is conceivable that a reservoir of the disease may exist in animals.

SANFORD, Chicago.

PHYSICAL TREATMENT OF PARALYSIS IN CHILDREN. R. G. GORDON and M. FORRESTER BROWN, Brit. J. Phys. Med. **9**:189 (Feb.) 1935.

The authors recommend complete rest for the active phase of the disease. Massage is an important procedure in cases of flaccid paralysis, reinforced with active and passive movements while the patient is immersed in a hot bath. In children electrical methods are used more as an aid to diagnosis and prognosis than for treatment. In cases of spastic paralysis the authors think that electrical treatment and massage are contraindicated. In these instances they use heat, passive movements and education, both motor and sensory.

HARTMAN, Cleveland.

THE DIAGNOSIS AND TREATMENT OF ABSCESS OF THE BRAIN. H. CAIRNS and C. DONALD, J. Laryng. & Otol. **50**:73 (Feb.) 1935.

Cairns and Donald in their discussion on abscess of the brain describe methods of operation and then analyze their own material, especially the cases in which failure resulted. They point out that abscesses of long duration usually have thick walls, and their experience shows that in these cases complete removal of the abscess and its wall is the only satisfactory treatment. Acute abscesses are not thick-walled, but they are rarely encountered at operation, and it is doubtful whether abscesses should be operated on in the acute stage. It is impossible to drain an area of acute purulent encephalitis, and it is probably unwise to disturb an abscess before it is localized. The diagnosis of abscess does not always indicate immediate operation. The authors further discuss the problem of locating an abscess, and they describe the method of exploration. They then discuss drainage by the closed and open methods. Whatever method is employed in the treatment of the abscess, the after-treatment is the same. The patient should be placed in such a position that gravity assists in drainage of the abscess. Dressings should be done only at long intervals. The first dressing should be left undisturbed as long as possible, usually about a week, sometimes ten days or even more, the dressing being changed only if a complication ensues or if the patient is becoming uncomfortable because of the discharge. After discussing postoperative complications the authors give their attention to the difficulties and mistakes in diagnosis and treatment. They show that many difficulties in diagnosis can be overcome by careful history taking and neurologic examination. They especially stress the importance of examining the visual fields. In each case of abscess there is need to form an estimate of when the abscess began and what stage it has reached, for this is the only way by which to gage the right moment for intervention. This can be done only by careful study of the history of the illness.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

INDUCED WATER RETENTION IN DIAGNOSIS OF IDIOPATHIC EPILEPSY. J. L. CLEGG and F. T. THORPE, Lancet **1**:1381 (June 15) 1935.

The authors repeated Jacobsen's procedure with sixteen adults suffering from epilepsy and seven persons not having epilepsy, used as controls. They conclude that this test is of definite value in arriving at a diagnosis in doubtful cases. No convulsion may be induced, however, when the patient has very infrequent seizures, and therefore a negative result is not conclusive. The water retention is accompanied by marked lowering of the osmotic pressure of the blood serum, and it is probable that the resulting exudation of fluid into the nerve tissues is the precipitating factor in the production of the seizures.

LANGMANN, New York.

POST-OPERATIVE INTRACRANIAL THROMBOSIS IN CHILDHOOD. P. R. EVANS, Lancet **2**:12 (July 6) 1935.

Postoperative intracranial thrombosis occurs rarely in childhood except as a local complication of mastoiditis. It occurs in cases of septicemia (usually streptococcic, and possibly of toxemia, by local spread from an infected air sinus and in cases in which there is no infection. Six cases from the autopsy records and two personally observed by the author are described. In four cases the operation was abdominal (in two instances, herniotomy), and in four cases, buccal (in three instances for the repair of cleft palate). In three of the last cases and in only one of the first group did infection occur. The superior longitudinal sinus was the most frequently involved.

LANGMANN, New York.

THE AUTONOMIC NERVOUS SYSTEM. H. J. WILKINSON, M. J. Australia **1**:801 (June 29) 1935.

Wilkinson gives a remarkably clear and concise account of the anatomy of the autonomic nervous system.

GONCE, Madison, Wis.

DETERMINATION OF FACIAL MOTORICITY IN YOUNG INFANTS BY THE KWINTE SCALE. IRENE MOURACHOWSKY, Arch. de psychol. **96**:338 (April) 1934.

Kwinte studied the voluntary facial motility of the child and listed the possible movements for each age period from 4 to 16 weeks. The author adopted Kwinte's gradations in a study of facial motility in children from 2 to 3½ years old. She observed one hundred and four children, fifty-three boys and fifty one-girls, who were divided in five groups. Of these 56 per cent were children of laborers, 30 per cent, of officials, 12 per cent, of military men and intellectual parents, and 2 per cent, of artists. They were divided into four age groups. For each child the physical and mental development was noted, the social milieu, the bodily conformation, the results of the Kuhlmann and Binet-Terman tests and the degree of facial motility. A comparative examination of the results shows that physical and mental development were always parallel in these children. Voluntary movements are the objective manifestations of steps decided on in the central nervous system. Voluntary facial movements in children from 2 to 3½ years of age are characterized by small amplitude and imperfect differentiation.

VINTON, New York.

POSTENCEPHALITIC OCULOGYRIC SPASM. E. ENGERTH, Deutsche Ztschr. f. Nervenh. **134**:191 (July) 1934.

Engerth reports a case of postencephalitic oculogyric spasm which was accompanied by peculiar manifestations. A boy, aged 17, had had an attack of encephalitis at the age of 10 years. For several years following this he appeared to be well except that he was more irritable and his school work was not up to its usual standard. At the age of 14 oculogyric attacks developed. Immediately before

and during such attacks, which lasted a few hours, there was a state of anxiety with obsessive ideas. The patient had a strong desire to run away from home. This, he thought, was the only way to bring about a permanent cure. At the same time he brooded over the fact that in this state he was unable to move. During the height of an attack he entertained ideas of suicide. Sleep terminated an attack. On awakening from such a sleep the patient felt perfectly well but was euphoric and had at times an irresistible desire to run away. Memory of his behavior during such a period was rather vague.

BERNIS, Rochester, N. Y. [ARCH. NEUROL. & PSYCHIAT.]

Psychology and Psychiatry

PSYCHIATRY AND THE PROBLEM OF DELINQUENCY. M. S. GREGORY, Am. J. Psychiat. **91**:773 (Jan.) 1935.

The psychiatrist's relationship to the problem of crime as it pertains to the study of the personality of the criminal is discussed. Studies of large numbers of criminals justify the classification of the following types: (1) Relatively normal delinquent persons, including those whose crime was committed under extreme circumstances. The childhood history reveals no marked deviation from the accepted standard of behavior. (2) Nonpsychopathic personality types, presenting occasional deviations, which are usually transitory. The group includes the neurotic, schizoid, paranoid, aggressive, egocentric, inadequate, shiftless, overconfident or overcompensating types of persons. (3) Psychopathic personality types, including persons with immature emotional development and neurotic manifestations, such as hysterical, schizoid, paranoid, cyclothymiac, epileptoid, hypomaniac and nomadic tendencies, and persons with constitutional and acquired physical inferiority and sexual abnormalities.

Psychiatry systematically applied to the study of these aberrations of conduct can do much in preventing the abnormalities and also in properly guiding the disposition of the criminal. Prevention of juvenile delinquency must be the major aim of the psychiatrist.

JAHR, Omaha.

INFLUENCE OF SIZE OF FAMILY UPON THE CHARACTERISTICS OF THE MENTAL DEFICIENT. NEIL A. DAYTON, Am. J. Psychiat. **91**:799 (Jan.) 1935.

A careful statistical study of 20,473 retarded children in the Massachusetts public schools is presented, with a discussion of the relationship between the size of the family and the intelligence quotient of the children examined, number of other siblings, grade-school accomplishments, standing in various subjects of the school curriculum, number of physical defects and occurrence of truancy and other problems of conduct and an evaluation of personality traits as they are related to the size of the family. The paper is profusely illustrated with graphs and tables. In summer, the following conclusions are made: Children of small families have a higher intelligence quotient than those of families of larger size. There is no particular tendency for large families to produce relatively larger numbers of retarded or mentally defective children. Children of small families show better accomplishments in reading and poorer aptitude for arithmetic. In language children from small and large families do better than those of families of intermediate size. There is a steady upward curve for the incidence of physical defects as the size of the family increases. "Normal conduct" is found more frequently in small than in large families, though stealing and sex offenses seem to show a higher incidence in the small families. "Lying" is more common in large families. Types of personality designated as obedient, social, stubborn, suggestible and quarrelsome occur more frequently in the larger families, while so-called emotionally unstable, seclusive, selfish, egotistic and over-affectionate children predominate in the smaller families.

JAHR, Omaha.

PALLIDAL AMENTIA. MARK S. REUBEN, Arch. Pediat. **52**:12 (Jan.) 1935.

Two cases of what the author calls pallidal amentia are reported, with a review of the literature on the subject. The author found that forty-five cases have been reported in the literature and that thirty-two of the reports are sufficiently comprehensive to permit classification and study of the cases. The article is concerned chiefly with the review of cases which have already been reported and with the report of two cases of the writer. The essential features of the disease appear to be as follows: The disease is thought to be congenital, with no history of birth trauma or rickets in a great majority of the cases. The children develop perfectly during the first four to six months of life, attaining the mental and physical powers corresponding to their ages. Without apparent cause bobbing of the head, salaam movements, *secousses* and general convulsions develop. The type of the seizures varies from time to time in the same child. There is gradual but progressive mental deterioration until complete amentia is reached. Muscular attainments are lost and much later regained. There may be transient paralysis and nystagmus. Symptoms referable to the cortical spinal tract are lacking; the head stops growing, and later the rate of growth is slower than normal, microcephaly being a distinct feature.

Roentgenograms reveal evidence of internal hydrocephalus, and the fundi are not affected. In the absence of complete autopsies, the exact pathologic features can be only surmised, but there is evidence that the cause of the condition is to be found in disturbance of the centers which release the pallidum. For this reason the author has termed the condition in these cases pallidal amentia.

WADDELL JR., University, Va.

MONGOLOID IMBECILITY IN THE NEGRO. ALWIN C. RAMBAR, Arch. Pediat. **52**:58 (Jan.) 1935.

The writer reports two cases of mongoloid imbecility in the Negro and calls attention to the infrequent reference to this condition in the literature. He finds that nine authors have reported a total of only twenty-two instances of mongoloid idiocy occurring in the Negro race.

WADDELL JR., University, Va.

AN ATTEMPT TO DETERMINE THE CONSISTENCY OF JUDGMENTS REGARDING THE ADJUSTMENT STATUS OF CHILDREN EXAMINED BY A CHILD GUIDANCE CLINIC. MABEL A. CARBERRY, J. Juvenile Research **19**:75 (April) 1935.

The technic is described and an evaluation is made of the reports of the adjustment status of children treated in behavior clinics. Parents, teachers and workers of the California Bureau of Juvenile Research gave independent opinions as to the effect of the treatment, and the percentages of agreements were determined. The conclusion is drawn that the best opinion of the rating is arrived at by a combination of the judgments of both parents, the teacher and some other worker in close contact with the child.

HAMILL, Chicago.

RESULTS OF REMEDIAL READING AT THE MIDDLE MORON LEVEL: A CASE STUDY. THORLIEF G. HEGGE, J. Juvenile Research **19**:128 (July) 1935.

This is the report of the results of remedial reading in a mentally retarded adolescent boy. A 13 year old boy was a frequent truant from school because of his difficulty in reading. The diagnosis was feeblemindedness and mental instability. He gave the impression of a physically perfect specimen, with good poise and pleasing personality. The intelligence quotient, according to the standard Binet test, was 59. However, "various performances were normal or supernormal." He was ambidextrous and a mirror writer. He was confused in oral reading. He received three hundred and thirty individual half-hour lessons in remedial training. During three years the intelligence quotient changed from 59 to 64,

and his reading ability increased from grade 2 to grade 5.5. Emotional factors that may have interfered with his reading ability were not discussed.

HAMILL, Chicago.

CHARACTERISTICS AND TRAINABILITY OF A CASE OF SPECIAL READING DISABILITY AT THE MORON LEVEL. RICHARD SEARS, J. Juvenile Research **19**:135 (July) 1935.

A boy had been in the training school for two and a half years and was almost a total "nonreader" but had reached the fourth grade in arithmetic. At the age of 17½ he had an intelligence quotient of 56 and was rather introverted. He received two hundred and fifty lessons during two years. He made considerable progress in individual word reading, especially at first, but in general his progress was unsatisfactory. However, it was said that he was very eager to learn, "but all attempts led to hopeless inaccuracy and confusion." There was no ocular imbalance; the word-reading ability was good; coordination of eyes and hands was normal, and ability in associated learning was good. It is stated that his inability to progress further was difficult to analyze. Among the difficulties was the influence of emotional inhibitions and a strong tendency to perseverate. As an illustration of the last-mentioned trait the following incident is of interest: "One day he read *luck* as *lunck*, reading—for him—rather hastily. He had previously been able to read this word correctly and had not shown any tendency to insert *n* in other words. However, once he made the mistake he seemed utterly unable to correct himself. He sounded the word slowly l-u-k, several times, but immediately afterwards would read it as *lunck*." Nothing said in the article leads one to suspect that there was anything specific in this instance. In my experience with children such a combination of letters as *u-c-k* is certain to suggest the tabooed word and cause mental difficulty, which may spread itself over any amount of territory. One wonders what the search for specificity among the emotional difficulties amounted to and how it was approached. It is certain that in learning words and in the play with words that have been learned the whole matter of good and bad may be involved. Also words are in a sense definitions, and if a word suggests certain things it may have to be changed to be acceptable. Is it possible that the *n* so changed the appearance and the meaning of this particular word to this boy as to make it more acceptable to him?

HAMILL, Chicago.

BEHAVIOR PROBLEMS OF THE PEDIATRICIAN. ESTHER L. RICHARDS, M. Clin. North America **18**:1663 (May) 1935.

With refreshing clarity and avoidance of psychologic jargon, Richards, within the compass of a few pages, outlines the diagnosis and management of some of the most frequently neglected problems arising in pediatric practice.

When one is confronted with a given case of "nerves" or "badness," the answers to the following questions must be determined: (1) What kind of constitutional stuff—intellectual, biologic and temperamental—is the child or the adolescent made of? (2) What environmental and educational process offers a given constitutional endowment its best chance of growth and development? These answers are to be sought by study of (1) the manner in which the child reacts to the environment of home and to group contacts and the grades obtained at school and (2) the results of scientific tests of intelligence and physiologic function. There are no such tests for emotional adaptation. The modern intelligence test is of outstanding value in the evaluation of mental health, and its application to the "lazy," the "indifferent" and the "bad" child yields many surprises. The child who is forced beyond his capacities may, if aggressive and energetic, turn to truancy or delinquency or, if shy and sensitive, retreat within himself, and nervous disorders, with a wide variation of symptoms, may develop. The first step in dealing with such a child must be to determine why he behaves as he does. If the abnormal behavior has a basis of intellectual incapacity, treatment logically lies in the attempt to fit the educational process to his handicap. There is, on the other hand, a large

group of children who possess an average or even a precocious intellectual endowment but who are hypersensitive not only to foreign proteins but to the strains of environment as well. To the last-mentioned condition they react as a protest by the development of stammering, bed-wetting, tics, asthma, mucous colitis and a great variety of functional disorders. At school, on account of their energy and eagerness to excel, they are often exploited, while at home music and dancing lessons add to the emotional unrest. The child soon learns how to utilize his neuropathic accomplishments in the control of uncomfortable environmental situations and to get what he wants. The problem facing the physician in such cases is, first, to recognize the factors underlying the child's abnormal behavior and, then, by directing his training within the limits imposed by fatigue, to teach him a reasonable control of his emotions and instincts.

Psychology divides the endowments of temperament into two groups, the outgoing and the ingrowing. The children possessing an excess of the outgoing disposition present the lesser problem, since their emotions and instinctive performances are objective and lend themselves to modification all along the way. The child with the ingrowing temperament, on the contrary, hides his problems and disguises his real emotions. Fantasy and day-dream supply emotional satisfaction rather than reality. A feeling of inadequacy, with an undercurrent of conscientious striving, keeps the personality ill at ease. For some persons the strain becomes too great, and they beat a slow retreat, ending in dementia praecox. Treatment of these conditions involves the early recognition of the temperamental ingredients of the endowment. Every possible effort should be made to make children of both temperaments aware of their respective possibilities for a reasonably all-around development of personality.

EUGENE SMITH, Ogden, Utah.

THE CHEMISTRY OF THE BRAIN IN THE MENTAL DEFECTIVE. W. R. ASHBY and ADA GLYNN, J. Neurol. & Psychopath. **15**:193 (Jan.) 1935.

Seventy-one brains, sixty-two of which were from mentally defective persons, were submitted to chemical analysis with a view to establishing whether the chemical constituents of the brain in patients with such disease are infantile and whether, since the histologic features of the cerebral cortex are difficult to assess objectively, chemical studies yield more direct information on the problem, as it is well known that chemical constituents of the brain undergo systematic changes in the course of development of the person.

The method of preparation of the brains and the chemical procedures are discussed, and the following results with conclusions are submitted: As the mental age increases the water content diminishes. Extracts show no variation. This is explained on the assumption that extracts represent myelin fairly closely, and so far as present data are available, the degree of myelinization in the mentally defective patient does not differ much from that in the normal person. The content of cholesterol, phosphatides and cerebrosides of these brains shows no significant change from that of the normal brain. The protein-phosphorus content is higher in the brains of defective patients than in those of normal persons, but the increase is only relative. This is explained by the fact that from birth to the mental age of 14 years the protein-phosphorus content per hundred grams decreases 9.2 per cent, while the weight of the brain increases 9.3 per cent. Therefore, the total quantity of nucleoprotein remains constant. Apparently, some other constituent of the brain increases with the mental age, thus producing a relative diminution in percentage of nucleoprotein.

The interpretation is also offered that "in the development of the brain the neuroblasts are at first small cells which consist mostly of nucleus with but little cytoplasm. As growth continues, the cells throw out more processes and thereby become relatively less nucleated. . . . Also, if the defective's nerve cells are held to be immature then our work suggests that the immaturity shows itself chiefly in the lack of cytoplasm rather than in any alterations in the amount of nuclear material." The following alternative explanation is suggested: Histologic

study shows that, on the whole, the neuroglial cells have less cytoplasm than the average nerve cell. The increase in the nucleoprotein content of the brain of the mentally defective patient may be due to a corresponding increase in the amount of neuroglia as compared with that of the normal cortex.

JAHR, Omaha.

PSYCHIC IMMUNITY AND UPBRINGING. J. K. FRIEDJUNG, Acta pædiat. **17**:411, 1935.

"To be healthy is to have the power not to react to everything"—*Nietzsche.*

The reviewer cannot repress a word of enthusiastic admiration for the neatness of the parallelism which Friedjung draws between somatic immunity against infection and psychic immunity to the attack of analogous foes. The body is protected in varying measure against the threatened invasion of infective agents by a variety of weapons. Some of these are on hand at birth; some are acquired in the battle with disease, and others are forged through the agency of prophylactic inoculation. If immunity is complete the invader is overcome promptly without appreciable embarrassment to the defender. If immunity is absent or defective a conflict follows, the repercussions of which are sensible to the defender. These repercussions constitute what is known as disease. The outcome of such encounters depends on the relative powers of the two contestants. With the present increasing perception of the unitarian nature of the individual, it becomes possible to look on psychologic phenomena from the point of view implied in the foregoing statements. A few of the bulwarks of equanimity may be present in the newly born infant; some are constructed automatically because of and through the agency of the exigencies of living; others are built up wittingly by the planned action of the child or by the efforts of his teachers. Looked at from this point of view, education, in the sense of rearing or bringing up, is the process of engendering psychic immunity.

The animal lives solely for the satisfaction of its instincts. By the employment of a system of reward and punishment certain animals may be made to adapt themselves to an artificial, man made environment. These adaptations are unstable, and atavism is common. The behavior pattern of the young of the human race is of a similar primitive character. Chronologically, the first function of education is to render the child sociable. From the standpoint of the infant, this process involves inhibition of his natural instincts. A "good" child is one who responds satisfactorily to the technic employed; a "bad" child is one whom violation of instinct renders recalcitrant and vengeful. As in animals, the equilibrium arrived at by this artificial conditioning is unstable. When restraining or retaining influences are removed, both the child and the adult tend to resume a behavior pattern more closely in keeping with their primitive instincts. A more rapid and violent reversion may occur in persons who have previously seemed to be firmly conditioned, when they are subjected to intolerable stress, such as the receiving of unmerited or injudicious punishment.

Education, as a process of interference with the fulfilment of natural instincts, may or may not result in the production of psychic immunity. Success in this respect implies that the pupil sooner or later takes over the task of his own instruction and becomes ultimately the master of his own instinctive desires.

The reliability of psychic immunity is subject to as many and as variable factors as is immunity to infection. The state of physical health is responsible for many of its fluctuations. Certain environmental influences may make the process of immunization difficult. The only child constitutes an illustration of this statement. The stoical person exemplifies psychic immunity in its most highly developed form. Finally, it is of peculiar importance to pediatricians to realize that many of the operations of psychic immunity in children are accompanied by symptoms which, at first glance, appear to arise from somatic disease. Prominent in this category may be habitual vomiting, refusal of food, diarrhea, stuttering, aphonia, mutism, convulsions, disorders of sleep, enuresis, fainting, palpitation, shortness of breath, running away and attempts at suicide.

MCCUNE, New York.

Diseases of the Genito-Urinary Tract

THE PRESENT STATUS OF VAGINITIS IN CHILDREN—A NEW TREATMENT METHOD. JOSEPH WRANA, Arch. Pediat. **52**:355 (May) 1935.

The types of vaginitis occurring in children are discussed, and suggestions for treatment are made. Attention is called to the necessity of an understanding of the histologic anatomy of the immature birth canal, an appreciation of the classification of vaginitis from an etiologic point of view and a knowledge of the pathologic anatomy of the bacterial, parasitic, chemical, thermal, mechanical and traumatic forms of vaginitis. As regards treatment, cleanliness is emphasized. To accomplish this end Wrana suggests the use of the ordinary apparatus of spray and suction as used by rhinolaryngologists.

WADDELL JR., University, Va.

RENAL TUBERCULOSIS; SOME MODERN CONCEPTS. ARTHUR J. GREENBURGER and MONROE E. GREENBERGER, Quart. Bull. Sea View Hosp. **1**:43 (Oct.) 1935.

In a series of 500 autopsies in a hospital for patients with tuberculosis, not a single patient showed a pathologic condition of the kidneys per se. However, such a condition is frequently secondary to pulmonary tuberculosis, since in this series of autopsies the kidney was involved in 252 instances. Hematogenous dissemination of tubercle bacilli frequently occurs in the pulmonary form of the disease, with involvement of the kidneys as well as of the liver and the spleen. Clinically, this form of the disease, the nondestructive closed type, is of little significance and is rarely accompanied by symptoms.

Unfortunately, destructive tubercular disease of the kidney presents few distinctive symptoms, and these are usually not discovered until the ureter and bladder become involved. When frequency of urination and dysuria are present and persist, a complete urologic examination is obligatory. The diagnosis is made by the recovery of the organism plus an alteration in the renal structure as demonstrated by pyelography.

The typical lesions are: (1) cortical necrosis ("moth-eaten appearance"), (2) irregular dilatation of the renal pelvis, (3) obliteration of one or more calices, (4) calicine abscess and (5) stricture of the ureter.

For nondestructive disease, in patients without urinary symptoms or changes in the pyelo-ureterogram, the authors recommend sanatorium care. For the destructive lesions, surgical treatment, as one step in the cure of tuberculosis, is advised.

EUGENE SMITH, Ogden, Utah.

TREATMENT OF THE UNDESCENDED TESTIS. E. D'ARCY MCCREA, Lancet **2**:753 (Oct. 5) 1935.

The sites of arrest in cases of undescended testis as usually described are: (1) the abdominal or supra-inguinal region, (2) the inguinal region and (3) the subinguinal region.

Maldescent predisposes to hernia, torsion, strangulation, trauma, tumor, hydrocele, inflammation and neurasthenia.

Four indications for operation are: (1) nondescent of both testes; (2) the presence of symptoms (e. g., pain or neurasthenia); (3) inguinal or subinguinal testis, and (4) coexistence of a hernia.

In cases of bilateral cryptorchidism, operation should be performed during the third or fourth year, and in cases of unilateral cryptorchidism, any time after the third year.

Transposition through the scrotal septum is recommended as the routine operation. If it should prove impracticable, the two stage Keetley-Torek operation is advised.

LANGMANN, New York.

THE URINARY SYNDROME AND THE RENAL FUNCTIONS IN HEMORRHAGIC NEPHRITIS OF CHILDREN. P. NOBÉCOURT and S. B. BRISKAS, Arch. de méd. d. enf. **38**:660 (Nov.) 1935.

A series of twenty-six cases of hemorrhagic nephritis in children between 2 and 13 years of age is reported in detail. Nineteen of the patients were boys, and 7 were girls. The authors' observations confirm the opinion generally held that the prognosis in hemorrhagic nephritis of childhood is favorable, at least as concerns life. They admit that certain invasions may be followed by humoral changes characterizing lipoid nephrosis. Edema is not common, while azotemia is the rule; this disappears between the fifteenth and the twentieth day. The cardiovascular syndrome is discrete.

AMESSE, Denver.

PYURIA. ALEXIO DE VASCONCELLOS, Arch. de pediat., Rio de Janeiro **7**:91 (Dec.) 1935.

Autogenous vaccines are efficient in the treatment of cystitis, pyelitis and pyelonephritis. Stock vaccines do not work as rapidly, nor are the results as sure.

SANFORD, Chicago.

TREATMENT OF PAROXYSMAL HEMOGLOBINURIA BY INOCULATION OF SPIROCHETA OF RAT BITE FEVER. K. SAKURAI, J. Pediat. (Tokyo), no. 420, May 20, 1935, p. 657.

The author treated four patients with paroxysmal hemoglobinuria by inoculation of the spirochete of rat-bite fever and reports a favorable therapeutic effect. In two cases there was no recurrence of the symptoms; in the other two cases there was marked improvement, although the Donath-Landsteiner reaction remained positive.

KATO, Chicago.

MYOMA UTERI IN PATIENTS UNDER TWENTY YEARS OF AGE. S. CLASON, Acta obst. et gynec. Scandinav. **15**:39, 1935.

Clason reviewed the literature in detail and found 16 instances belonging to this group. He adds his own case of a patient 16 years of age and discusses it in detail.

There was a history of amenorrhea for six months, associated with pain, and finally hemorrhage. Examination showed a tumor protruding 4 fingerbreadths above the symphysis, the size of a child's head, pushing down the anterior vaginal wall. Behind the mass a uterus of normal size seemed to exist. The patient was exceedingly anemic.

The diagnosis of ovarian tumor was made and the patient was operated on. Myoma was not taken into consideration because of the patient's age. Laparotomy revealed a single myoma in the posterior uterine wall, about the size of a large orange. There was an uneventful recovery.

ADAIR and POTEKIN, Chicago.

A CASE OF RENAL RICKETS. J. T. VAN DER HOEVEN, Maandschr. v. kindergeneesk. **4**:333 (May) 1935.

A boy of 6 years, who was much too small and too light for his age, had all the classic symptoms of severe rickets. The calcium content of the blood was normal; the phosphorus content was somewhat increased. There was slight albuminuria, with no casts. Kidney function tests showed a great insufficiency of the kidneys, which probably was congenital.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of the Ductless Glands; Endocrinology

AN INSTANCE OF MARKED ABDOMINAL DISTENSION WITH THE PROBABLE ETIOLOGIC FACTOR BEING ABNORMAL ENDOCRINE FUNCTION. GEORGE B. DORFF, Am. J. Digest. Dis. & Nutrition **2**:328 (July) 1935.

Dorff cites a case of a 6½ year old boy who had marked abdominal distention. Roentgenograms of bones showed delayed ossification centers, and roentgen studies of the intestines showed marked atonia. After therapy with desiccated thyroid the abdominal distention decreased and the roentgen studies of the intestines showed an increased intestinal tone.

MORRISON, Savannah, Ga.

RELATION OF THE CUSHING SYNDROME TO THE PARS INTERMEDIA OF THE HYPOPHYSIS. W. G. MCCALLUM, T. B. FUTCHER, G. LYMAN DUFF and READ ELLSWORTH, Bull. Johns Hopkins Hosp. **56**:350 (June) 1935.

A typical case of the Cushing syndrome (obesity of the face and trunk, cutaneous striae, osteoporosis, hypertension, diabetes and cessation of gonadal function) is described. Anatomically, there was a basophilic adenoma of the hypophysis, which the authors conclude was derived from the cells of the pars intermedia. In the present state of knowledge it is impossible to offer any satisfactory explanation of the profound disturbances in function which accompany these tumors.

LYTTLE, New York.

CLINICAL OBSERVATIONS ON THE EFFECTS OF APL (ANTUITRIN-S) ON THE TESTICLE. W. L. BROSIUS, Endocrinology **19**:69 (Jan.-Feb.) 1935.

The usual management of cryptorchidism has been surgical. Schapiro treated thirteen subjects with this condition with the gonadotropic hormone from the urine of pregnant women and reported improvement in all. Engle hastened the descent of testes in immature monkeys by the administration of this hormone. Sexton reported treatment of six boys who had cryptorchidism; in four there was complete descent. On the basis of these reports the treatment of the nine patients reported on in this paper was undertaken.

The boys ranged in age from 3 to 15 years. The gonadotropic hormone was given in doses varying from 1 to 3 cc. at intervals of from one to three times weekly. In one case daily injections of 1.5 cc. were given for ten days, followed by 3 cc. daily for fifteen days.

In five of the cases desiccated thyroid gland, ½ grain (0.03 Gm.) was given twice daily and in one, thyroid to tolerance.

Following the treatment there was complete descent in six cases. In two cases partial descent was obtained. In one case the treatment was without demonstrable effect.

Data on twelve cases of sterility in males, indicating the beneficial effect of treatment with the gonadotropic hormone from the urine of pregnant women, are also reported.

JACOBSEN, Buffalo.

A CASE OF PITUITARY INFANTILISM TREATED WITH COMMERCIAL ANTERIOR PITUITARY PREPARATIONS. GEORGE B. DORFF, Endocrinology **19**:209 (March-April) 1935.

Since the treatment of pituitary infantilism is still in the experimental stage, interest attaches to any success achieved.

A boy, aged 16 years, complained of dwarfism, lack of genital development and asthma. He was backward in bony development as evidenced by delay in closure of certain epiphyses. His height was 57 inches (144.8 cm.), the average normal height being from 61⅘ to 66⅕ inches (156.9 to 168.1 cm.). His genitalia showed the presence of two small testes in the scrotum; the penis was small, and there were a few fine fuzzy pubic hairs. The appearance of the patient was eunuchoid. A diagnosis of pituitary infantilism of the Levi-Lorain type was made.

His height had remained stationary for a number of years. Under treatment with commercial anterior pituitary preparations (injections three times a week of 1 cc. of unfractionated anterior pituitary extract up to forty-three doses and, later, injections of an extract containing the growth hormone in similar doses to a total amount of 30 cc., he grew 3¼ inches (8.3 cm.) in height and gained 11½ pounds (5.2 Kg.) in eighteen months. The genitalia showed great improvement in size, and a marked crop of pubic hair appeared. His mental attitude completely changed.

That delay in puberty would have terminated and puberal changes would have occurred naturally if no treatment had been given must be considered. However this is improbable, because the boy for a number of years had shown neither growth nor sexual development, then suddenly achieved both within a comparatively short period.

JACOBSEN, Buffalo.

ENDOCRINE DISORDERS IN CHILDREN WITH PARTICULAR REFERENCE TO TREATMENT. RALPH H. KUNSTADTER, M. Clin. North America **18**:1443 (March) 1935.

The diagnosis of hypothyroidism should be considered in all infants and children showing retarded skeletal growth and roentgenographic evidence of delayed ossification. Other symptoms suggestive of this condition are lowered body metabolism; mental retardation; a cold, dry, rough skin; dry, coarse and brittle hair, a coarse voice and an enlarged abdomen. General obesity with supraclavicular fat pads is frequently present. The blood cholesterol level may be elevated and bear a reciprocal relation to the basal metabolic rate. This observation is of especial value in young children on whom it is difficult to obtain accurate results of metabolic tests. It has also been found that there is a decrease or complete cessation of excretion of creatine in hypothyroidism, which may be restored to normal by thyroid medication. This finding is of great value in treatment, since under thyroid therapy creatinuria appears before any change is noted in the basal metabolism and the blood cholesterol content. The appetite of the child with hypothyroidism is usually poor, and as a consequence the intake of iron and calcium is likely to be deficient. It is therefore necessary to supply these elements medicinally, as well as iodine, during the adolescent period.

Fröhlich's syndrome is the most common form of juvenile hypopituitarism. It is recognized by the presence of the girdle deposit of fat, a soft velvety skin, retarded sexual development and a tendency to female configuration. The intelligence is good, but the temperament is usually lazy and placid. Obese patients should be given a low caloric, high protein diet. Those with a low metabolic rate should receive thyroid gland. Large doses of desiccated anterior lobe (Kundstadter) of the pituitary gland are of value in some cases. The author has given the anterior pituitary-like gonadotropic hormone from the urine of pregnant women hypodermically in a series of cases and was favorably impressed with the results obtained.

Several less common endocrine disorders affecting children, including diabetes insipidus and the clinical syndromes of precocious puberty and virilism, are briefly treated in this paper.

EUGENE SMITH, Ogden, Utah.

THE DIETARY MANAGEMENT OF DIABETICS AT THE DIABETIC CLINIC OF THE INFANTS' AND CHILDREN'S HOSPITALS, BOSTON, MASS. ALLAN M. BUTLER, New England J. Med. **212**:760 (April 25) 1935.

Butler's observations are based on the following premises: 1. Almost all children with diabetes require insulin if their physical condition is to be such as to permit their leading normal lives. 2. Diets of excessively high or low caloric value should be avoided. 3. The use of low carbohydrate, low protein and high fat diets are no longer necessary. 4. There are certain advantages in a liberal carbohydrate diet and no demonstrable contraindications. (*a*) The blood fat and

cholesterol contents are kept within normal limits. (*b*) The child eats food more nearly like that of others about him, and the temptation to take food outside of that prescribed is less. These two results are of psychologic importance. (*c*) With the onset of an infection the dietary management is easier when the patient is on the liberal carbohydrate diet than when he is on the high fat diet. 5. Diabetic children usually do better when they show a trace of sugar than when on a regimen that renders their twenty-four hour specimen of urine continuously free from sugar.

The dietary instructions to all diabetic persons over 2 years of age are as follows: (*a*) Eat no candy, cakes, cookies, jams or sugar and no desserts to which such ingredients have been added in any considerable amount. (*b*) Eat but one piece of bread a meal or its equivalent in crackers. (*c*) Have at one meal only one of the following: rice, macaroni or potato, and of the one take only one moderate helping. (*d*) Eat but half a banana or apple at any one time. (*e*) In the middle of the morning take some form of food containing between 10 and 20 Gm. of carbohydrate. If at any time symptoms of hypoglycemia appear, the juice of one orange or some food containing 10 Gm. of dextrose is to be taken immediately. (*f*) Except for these instructions, eat as desired at meal-time, provided ordinary common sense is applied in not stuffing on any particular dish.

With such a regimen, insulin is given in sufficient amounts and appropriate distribution to render the patient almost free from sugar and free from hypoglycemic periods. The institution of this regimen has lessened the period of hospitalization of these patients markedly. Untreated patients entering the hospital may be adjusted to diet and insulin within from three to six days and are discharged to the outpatient department or the care of their private physician, and final adjustments to home conditions are made during the next week.

GENGENBACH, Denver.

ANTERIOR-PITUITARY DWARFISM: FURTHER REPORT OF CASES TREATED WITH THE GROWTH HORMONE. HENRY H. TURNER, South. M. J. **28**:309 (April) 1935.

Turner reports that the growth hormone is evidently potent in stimulating growth in certain selected cases of endocrine dwarfism. In its present potency the frequent administration of the necessarily large doses militates against its general clinical use. There is a possibility of the establishment of a physiologic resistance, or antihormone response, from continued administration of this hormone.

SCHLUTZ, Chicago.

PITUITARY DISORDERS IN CHILDHOOD. H. GARDINER-HILL, Practitioner **134**:480 (April) 1935.

Pituitary disorders in childhood give rise to disturbances of growth, sex development and metabolism from abnormal function of the different cell groups in the gland. The clinical picture varies widely. Both hypopituitary and hyperpituitary conditions have been described. The picture in preadolescent hyperpituitarism is not clearcut, and the underlying pathology has not been completely worked out. Hypopituitarism is much better understood.

In discussing criteria for diagnosis the author points out the importance of: (*a*) growth and skeletal defects, (*b*) osseous development, (*c*) compression symptoms due to tumors and (*d*) the normal mentality.

The main types of hypopituitarism are presented: One is so-called Simmond's disease, in which there is destruction of the anterior lobe due to ischemic necrosis —the end-result of infarction; the other is Fröhlich's disease, in which the pathologic changes are due to a parahypophysial tumor. Several illustrative cases are presented.

Pituitary basophilia is also discussed, and illustrative cases are given.

SAPPINGTON, San Francisco.

HYPERTHYROIDISM DATING FROM INFANCY. R. W. B. ELLIS, Proc. Roy. Soc. Med. **28**:832 (May) 1935.

A case of this condition in a girl of 14 years is reported. The patient's mother said that the child had had marked exophthalmos since birth and that throughout childhood she had been very nervous. At the age of 10 years she was treated as an outpatient under Dr. Patterson and was reported on at that time. She had a palpable thyroid and tachycardia. Since the age of 8 years she has suffered from petit mal. She was treated with arsenic, bromides and iodine, and for eighteen months she was quieter and the exophthalmos was less marked. At the age of 14 she was well developed and had menstruated for fifteen months. There was still fulness of the thyroid, with a fine tremor of the hands and a slight degree of exophthalmos. Von Graefe's and Stellwag's signs were present. The report is accompanied by a picture of the patient and comment by the author.

WILLIAMSON, New Orleans.

ENDEMIC GOITRE IN THE LANGKLOOF VALLEY. E. E. BUTTNER, South African M. J. **9**:187 (March 23) 1935.

The incidence of goiter in man and farm animals in the Langkloof Valley is extremely high. Contributing factors to this high incidence of goiter are: (1) the high calcium content of the soil, vegetation and water, (2) the low phosphorus content of the soil and vegetation, (3) the low iodine content of the food ingested by the inhabitants and (4) insufficient sunshine. The phosphorus deficiency in the presence of excess of calcium results in conditions which render the iodine absorbed from the food unavailable to the tissues.

GONCE, Madison, Wis.

FUNCTION OF THE PARATHYROID GLANDS. GEORG LENART, Ergebn. d. inn. Med. u. Kinderh. **46**:350, 1934.

This article is a lengthy review of the morphology, physiology, pathology and function of the parathyroid glands. It represents chiefly a summation of the present knowledge on the subject and a compilation of the current views.

CAPPER, Philadelphia.

THYMIC HYPERPLASIA AND THE SEASON. H. SCHONFELD, Monatschr. f. Kinderh. **63**:33, 1935.

Schonfeld presents reports of cases, illustrated with seven roentgenograms, to show that hyperplasia of the thymus is related to the season of the year. In the cases reported it seemed to reach its maximum during spring.

GERSTLEY, Chicago.

THE DOSE OF THYROID IN MYXEDEMA. L. KENA-APAJALAHTI, Acta pædiat. **17**:398, 1935.

With few exceptions, the contemporary methods of treating myxedema place too great emphasis on the importance of avoiding overdoses of thyroid preparations. This attitude arises from an unfounded fear of producing symptoms of thyrotoxicosis. The principal corollary of such an apprehensive frame of mind is that the criteria of success in the treatment of severe thyroid deficiency are not high enough. Many physicians are satisfied if the purely physical stigmas of myxedema are obviated or improved, even though the mental development of the patient remains at a relatively low level.

Patients with severe cases of myxedema require much larger daily doses of thyroid than have been generally employed heretofore. There is little danger of overtreatment. Whereas inadequate therapy may provoke symptoms of hyperthyroidism, such manifestations disappear when the dose of thyroid is increased to the optimal amount.

The author reports four cases of hypothyroidism of different degrees of severity which were treated in the University Children's Clinic, Helsingfors. The optimal daily dose for patients of various ages was found to be as follows:

½ year to 1 year	0.45–0.70 Gm.
9 years	0.90–1.20 Gm.
26 years	1.20–1.50 Gm.

One patient, 26 years of age, received from 6 to 6.5 mg. of thyroxin daily in addition to thyroid, without manifesting symptoms of toxicosis.

McCUNE, New York.

IODINE CONTENT IN FOODSTUFFS IN RELATION TO GOITER. P. A. MEERBURG, Nederl. tijdschr. v. geneesk. **79**:3289 (July 6) 1935.

The iodine content in foodstuffs is, as a rule, insufficient to guarantee a daily supply of from 80 to 100 micrograms of iodine. This amount is necessary to prevent enlargement of the thyroid gland and is only a prophylactic dose. The iodine content of foodstuffs may be increased in two ways: first, by adding iodine to foodstuffs and, second, by giving to animals the products of which are used food that is rich in iodine (as to cows for increasing the iodine content of the milk and to poultry for making the egg richer in iodine).

VAN CREVELD, Amsterdam, Netherlands.

Diseases of the Muscles, Bones, Joints and Lymph Glands

ANOTHER CASE OF "PULLEY VERTEBRA." R. YVIN, Bull. off. Soc. franç. d'électrothérap. **44**:255 (May) 1935.

A lateral roentgenogram of a 7 year old boy with Pott's disease showed all the dorsal vertebrae to have the "pulley" deformity. The twelfth dorsal vertebra was reduced to a mere scale of bone; the upper surface of the first lumbar vertebra was concave, and the tenth dorsal vertebra was indented by notched osteitic areas.

VINTON, New York.

PIGMENTED SPOTS AND OSSEOUS LESIONS (ABORTIVE FORMS OF NEUROFIBROMATOSIS). H. GRENET, R. DUCROQUET, P. ISAAC GEORGES and M. MACÉ, Bull. Soc. de pédiat. de Paris **32**:158 (March) 1934.

Thirteen patients showing café au lait spots on the skin and skeletal deformities due to osseous malformations were observed in a year. Many of the bony anomalies were congenital, and some were acquired. In a number of instances these two abnormalities were present in several members of the same family. The cases were considered to be instances of neurofibromatosis, even though no neurofibromas were present. It is pointed out that bony malformations constitute a part of the picture in Recklinghausen's disease. They are of greater significance and often less amenable to treatment when associated with pigmented spots of the skin than is sometimes recognized; this is true especially of scoliosis. The children may later show typical neurofibromas, and frequently definite neurofibromatous lesions may be found in older members of the family if a careful search for them is made.

BENJAMIN, Montreal, Canada.

MULTIPLE CHONDROMAS ASSOCIATED WITH SUBCUTANEOUS FIBROMAS AND SCLERODERMA. E. LESNÉ, C. LAUNAY and G. LOISEL, Bull. Soc. de pédiat. de Paris **32**:667 (Dec.) 1934.

A boy of 8 years presented a number of connective tissue disturbances, consisting of chondromas of the phalanges and of the left ear, subcutaneous fibromas

where the skin had been the seat of trauma or infection, sclerodermatous plaques and sclerodactylia. The cholesterol, uric acid, phosphorus and calcium contents of the blood were normal. The basal metabolic rate was minus 15 per cent, but there was no clinical evidence of hypothyroidism.

BENJAMIN, Montreal, Canada.

PRIMARY ACUTE OSTEOMYELITIS OF THE PATELLA. RIGAUX and MILHIET, Progrès méd., April 13, 1935, p. 613.

A case of osteomyelitis of the patella in a boy 9 years of age is reported. The condition is rare; it is most frequent between the ages of 8 and 12 years, when vascularization of the patella occurs. The pain is extreme, and the leg is held in a position of extension. The temperature is high. Sequestrums are usually found at operation. The prognosis is good. In the case reported there was complete recovery.

LESLIE, Evanston, Ill.

ACUTE OSTEOMYELITIS OF THE MEDULLARY CANAL. MARCEL FÈVRE, Rev. d'orthop. **22**:105 (March) 1935.

Acute central osteomyelitis may be classified under three heads: (1) the typical form, (2) the septic-pyogenic form and (3) the septic form. In the first type, trephining into the medullary canal results in cure. In the second type, trephining helps, and in the third form the infection must be attacked from the general angle, since the condition is widespread. Operation in this form depends on the degree of the local infection in the bone. In the author's opinion, whenever osteomyelitis is diagnosed and is localized, operation should be undertaken. If no pus is found subperiosteally, trephining should be done, even if the bone appears healthy.

RYAN, Vancouver, Canada.

PROGRESSIVE MYOSITIS OSSIFICANS; REPORT OF A CASE. M. YVIN, Rev. d'orthop. **22**:135 (March) 1935.

A child 4½ years of age was seen in 1933 because of a condition which was diagnosed as Pott's disease of the twelfth dorsal vertebra. She was one of ten children; all the others were healthy except one sister, who had had a dislocation of the hip. This child walked at the age of 13 months and appeared healthy until 1931, at which time she had an undiagnosed illness lasting fifteen days. In December of that year it was noticed that she was unable to raise the arms above her head. In July 1932 Pott's disease was first diagnosed. On admission to the hospital in 1933, roentgenograms were taken which showed beginning calcification about the right shoulder joint. The child was given 0.005 Gm. of parathyroid extract and 0.1 Gm. of epinephrine without any noticeable effect. In December 1933, tenotomy of the right and left latissimus dorsi muscle and right pectoralis major muscle (lower fibers) was done. After this operation the child could again raise her arms, but the range of motion gradually decreased, and a roentgenogram taken in February 1934 showed progressive ossification extending throughout the scar tissue resulting from the tenotomy.

RYAN, Vancouver, Canada.

HISTOLOGIC STRUCTURE OF TEMPORAL BONE IN CONGENITAL AND LATE OSTEOGENESIS IMPERFECTA. F. ALTMANN, Monatschr. f. Ohrenh. **69**:448 (April) 1935.

Altmann points out that osteogenesis imperfecta is a disease of the entire skeletal system and becomes manifest in a disturbance of the endochondral as well as of the periosteal ossification. It is essentially the result of a deficient

function of the osteoblasts, probably on the basis of a defect of the formative power of the entire mesenchyma. Like the other generalized skeletal diseases, osteogenesis imperfecta becomes manifest also on the temporal bone; and the bony labyrinthine capsule, because of its peculiar development and structure, is well suited for the study of the pathogenesis of the disease. After mentioning several other investigators who have made histologic studies on the temporal bone in cases of osteogenesis imperfecta and after briefly reviewing their observations, Altmann describes his own studies. The first temporal bones studied by him were from a new-born girl with the typical aspects of osteogenesis imperfecta, with changes in the entire skeletal system and with multiple fractures. Following embedding of the temporal bones in pyroxylin (celloidin) the right one was sectioned vertically and the left one horizontally. The temporal bones showed the changes which are characteristic of osteogenesis imperfecta and which were observable also in the other portions of the skeleton. There were quantitative as well as qualitative changes in the bone formation. The quantitative changes were found in all portions of the temporal bone. The endosteal layer of the bony labyrinthine capsule showed a decrease in mass only in the upper portion of the cochlea. The changes in the periosteal layer were more noticeable, but the endochondral layer showed the severest changes. Here the reduction in the mass of the bone tissue had resulted in a greater width of the medullary spaces. The reduction in the mass of the bone tissue was more noticeable in the posterior portions of the vestibule and of the semicircular canals than in the region of the cochlea. The author, like Fischer, Weber and Mayer before him, observed that the spaces of the vestibule and of the semicircular canals were surrounded by a layer of extraordinarily compact bone, which was adjoined by the medullary space with its scant and thin trabeculae. The reduction in mass of the endochondral and periosteal bone tissues and the width of the central medullary space were noticeable also on the malleus and the incus. Regarding the qualitative changes, the author states that the fibrillar structure of the endochondral bone tissue corresponds to the strandlike bone tissue and shows a greater abundance of roundish bone cells than is usually the case. However, these changes are not uniform throughout, but are more noticeable on the posterior portions of the labyrinthine capsule, particularly in the region of the semicircular canals, than on the cochlea. Like Fischer and Meyer, the author was able to detect in some parts, particularly in the upper portions of the cochlea, unusually large cartilaginous rests, but he also observed in this region somewhat larger interglobular spaces. In the zones of ossification, he observed, like Meyer, some irregularities in the decomposition of the cartilage. The estimation of the periosteal tissue proved difficult, because it normally undergoes considerable changes during this period of development. The endosteal bone tissue showed almost normal structure. The author calls especial attention to a formation in the anterior portion of the right middle ear, which, on the basis of its histologic structure, must be regarded as an arterial remnant, and he considers it possible that the formation is a remnant of the arteria stapedia. He further describes studies on the temporal bones of a female infant of premature birth (eighth lunar month) with typical osteogenesis imperfecta. In this case, too, there were quantitative and qualitative disturbances in the bone formation. Then, after pointing out that osteogenesis imperfecta appears not only in fetuses but also in children and adults, the author states that Ruttin studied the late form in a patient aged 24, and that he himself was able to study the juvenile form in a child aged 17 months. He gives a detailed description of his histologic studies in this case. In the conclusion he agrees with Bauer, who regarded the congenital form of osteogenesis imperfecta as the defective ossification of the developing bone and the late form as that of the growing bone. He also concurs with Tanturri, who called attention to the greater incidence of osteogenesis imperfecta in females.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

Diseases of the Eye

JUVENILE MACULAR EXUDATIVE RETINITIS (JUNIUS). W. T. DAVIS and ERNEST SHEPPARD, Arch. Ophth. **13**:960 (June) 1935.

Much confusion exists as to the classification and etiology of macular disease. Coats' disease is rather definitely known. Junius has described what he calls juvenile macular exudative retinitis, a lesion at the macula. The diagnosis may be based on the youth of the patient, negative medical findings, chronicity without great reduction of vision, final recovery of normal vision and the absence of hemorrhages.

WESCOTT, Chicago.

BILATERAL RETINAL GLIOMA TREATED BY RADIATION: CLINICAL AND HISTOLOGIC REPORT. A. G. FEWELL and W. E. FRY, Arch. Ophth. **14**:190 (Aug.) 1935.

Fewell and Fry state the belief that the present opinion in regard to glioma of the retina indicates that in the presence of an unaffected eye with useful vision, the affected eye should be enucleated, but in cases of bilateral involvement in which one eye retains useful vision and in which ophthalmoscopic examination indicates that in all probability the optic nerve head is not involved, the proper procedure would be enucleation of the first eye with irradiation of the second.

The authors report a case of glioma of the right eye with a smaller tumor of the left eye. The right eye was enucleated, and the left eye was submitted to roentgen therapy. Two new nodules had developed below the disk. At first the lesions regressed, but later the entire vitreous became filled, and the second eye was enucleated.

WESCOTT, Chicago.

CONGENITAL BILATERAL MELANOSIS OCCURRING IN THE EYE AND FACE: A CONTRIBUTION TO THE PROBLEM OF CONSANGUINITY. P. KIEWE and I. MANEFF, Ann. d'ocul. **172**:723 (Sept.) 1935.

Ocular hyperpigmentation has interested ophthalmologists at all times, and their interest has increased with the study of hereditary conditions of the eye. The number of cases in which pigmentation has been proved to have a hereditary origin are few. Franceschetti (Schieck and Brückner) noted only three publications on cases of hereditary pigmentation of the eye: those of Bourquin, Fleischer and Selter.

The case reported is that of an adult man, 64 years of age, who had marked pigmented areas over the face, especially about the eyes. The lids in particular were pigmented, especially along the edges, where there were fine brownish-black spots that tended to come together. The palpebral conjunctiva presented a similar picture, and the deeper parts were more involved than the superficial. Examination with the slit lamp showed the pigmentation to be in the subepithelial layer. The cornea presented only arcus senilis. General examination revealed nothing of interest except a pigmentation on the trunk and extremities similar to that of the face. A son of this patient, a boy of 8 years, presented a similar condition.

The article is illustrated with a good photograph of the patient, colored drawings of the lesions in the skin and a chart illustrating the consanguineous relationship in such cases.

MCKEE, Montreal, Canada. [ARCH. OPHTH.]

BERNARD-HORNER (HORNER) SYNDROME. BUONOCORE PASQUALE, Pediatria **43**:568 (May) 1935.

A case of Horner's syndrome in a girl of 8 years is reported, in which the syndrome coexisted with a specific pulmonary lesion.

Attention is directed to the rarity of the condition, and, in the author's case, to the presence of congenital megalophthalmus and megalocornea. The author suggests that the syndrome may have been brought about by stimulation of the cervicothoracic section of the sympathetic system by these congenital anomalies.

SIGNORELLI, New Orleans.

Ectopia of the Lens. Benito Just Triscornia, Arch. de oftal. de Buenos Aires **10**:251 (April-May) 1935.

After limiting, with Fuchs, the name "lenticular ectopia" to congenital subluxations, mostly bilateral, symmetrical and hereditary, and after stressing their rarity, the author reports a case in which no data on the heredity were obtainable.

Finlay, Havana, Cuba. [Arch. Ophth.]

Dacryocystitis of the New-Born. Pérez Bufill, Arch. de oftal. hispano-am. **35**:345 (July) 1935.

After an anatomic description of the different parts of the excretory lacrimal apparatus, with attention to certain embryologic peculiarities, the author discusses the dacryocystitis occurring in the new-born infant due primarily to nondislodgment of the epithelial plug occupying the lacrimal canal and to secondary infection of the retained tears. The prognosis depends on the degree of the infection. In connection with the treatment he recommends exclusive careful catheterization without prior slitting of the puncta or canaliculi, supplemented in cases in which there is much secretion by irrigation with mild antiseptic solutions. He briefly reports 20 cases in which cure was obtained with from three to sixteen catheterizations and refers to 328 additional cases not reported here.

Finlay, Havana, Cuba. [Arch. Ophth.]

Primary Tuberculous Infection of the Eyelid. Popovici-Lupa, Vasile Petresco-Coman and C. Vasilesou, Monatschr. f. Kinderh. **63**:359, 1935.

The case of a 4 year old infant with a primary tuberculous focus in the eyelid is reported, and a photograph and two photomicrographs of a histologic specimen are shown. Death occurred later from generalized tuberculosis.

Gerstley, Chicago.

Skin Diseases; Allergy

Studies on the Relation of the Adrenal Glands to Allergic Phenomena: III. On the Specific Therapeutic Effects of Cortical Adrenal Extract in Asthma. Milton B. Cohen and J. A. Rudolph, J. Allergy **6**:279 (March) 1935.

A preparation of cortical adrenal extract of known potency used on four patients with chronic asthma had no significant specific effect on the condition.

Hoyer, Cincinnati.

Orris Root Fingers. Louis E. Prickman, J. Allergy **6**:302 (March) 1935.

Prickman calls attention to the fact that orris root fingers, which are frequently used as a necklace for children who are teething, may be a possible source of sensitivity to this substance, and believes that their use should be discouraged in allergic families.

Hoyer, Cincinnati.

The Significance of Tobacco Reactions in Allergic Children. Robert Chobot, J. Allergy **6**:383 (May) 1935.

Only six, or 11 per cent, of fifty-three unselected asthmatic children had negative skin reactions when tested with tobacco extract. Of those who showed negative reactions to tobacco extract, three gave other skin reactions.

The children ranged in age from 3 to 12 years and had never smoked, their contact with tobacco having been only casual.

Hoyer, Cincinnati.

Studies on the Relation of the Adrenal Glands to Allergic Phenomena: II. The Therapeutic Effect of Strychnin Stimulation of the Adrenal Medulla in Asthma. Milton B. Cohen and J. A. Rudolph, J. Allergy **6**:404 (May) 1935.

Strychnine sulfate, from 1/12 to 1/6 grain (0.005 to 0.01 Gm.) was given to four asthmatic patients. Hypertonicity developed in one-half hour, with relief of symptoms of asthma within an hour; however by this time the effect of the strychnine was so great that slight movement caused reflex spasm of the respiratory muscles, producing extreme dyspnea.

The strychnine apparently increased the output of epinephrine, but the amount required to give relief from the asthma is not useful clinically.

Hoyer, Cincinnati.

Inhalation of Epinephrine for the Relief of Asthmatic Symptoms. James B. Graeser and Albert H. Rowe, J. Allergy **6**:415 (July) 1935.

Beneficial results were obtained in a group of asthmatic patients by inhalation of a 1:100 solution of epinephrine from a specially made nebulizer. The solution and nebulizer will be made available for general use. It will be necessary to be cautious in the use of epinephrine in this way, since the dose cannot be measured, and the patient will have to be warned to proceed slowly until the individual requirement can be ascertained.

Hoyer, Cincinnati.

Oral Desensitization to Common Foods. Beatrice M. Keston, Irene Waters and J. Gardner Hopkins, J. Allergy **6**:431 (July) 1935.

The method of making dilutions of the more common foods is given. The first dilution is calculated to make the initial dose contain 1 mg. of protein. The dose is increased every four days. If symptoms recur the dose is decreased to that of twelve or sixteen days previous. If the symptoms continue the desensitization is discontinued until they subside.

The method has been used successively for five years in desensitizing persons sensitive to the common foods, especially children with chronic allergic eczema.

Any one interested in this subject should send to the author for a reprint. It is said to contain lists of foods to be avoided during desensitization. These lists are omitted from the article because of their length.

Hoyer, Cincinnati.

A New Method for Covering Pillows. Gerald C. Grout, J. Allergy **6**:507 (July) 1935.

Liquid rubber or latex is painted on the outside of a pillow or mattress with an ordinary paint-brush. This has been found to be very effective in preventing symptoms which were caused previous to painting the pillow.

Hoyer, Cincinnati.

Malignant Melanoma (Black Cancer). Kenneth M. Lynch, J. South Carolina M. A. **31**:129 (July) 1935.

Lynch cites several cases of pigmented nodules, which are neoplasms. Request is made to be on the lookout for this condition. Early diagnosis and complete removal are the only way of preventing black cancer.

Weston Jr., Columbia, S. C.

A Clinical Evaluation of the Positive Skin Reaction in Asthma, Urticaria, Vasomotor Rhinitis and Seasonal Hay Fever. Abraham Colmes, New England J. Med. **212**:725 (April 18) 1935.

The data here presented were obtained from the records of 250 patients with bronchial asthma, 93 with urticaria, 222 with perennial vasomotor rhinitis and

314 with seasonal hay fever. In asthma, more positive reactions occurred to inhalants than to foods (935 and 750, respectively); 53 per cent of the reacting inhalants and only 25 per cent of the reacting foods were of etiologic significance. In urticaria, the specific allergen was discovered more than twice as often through the history of the patient or through trial and error diets than through skin tests (74 and 34 times, respectively).

While the ratio of the foods causing reactions to inhalants causing reactions in the group with vasomotor rhinitis was 1:1.6 (345 and 562 reactions, respectively), the corresponding ratio of their clinical importance was 1:8 (25 and 202 reactions, respectively).

Of 314 patients with seasonal hay fever, 310 (nearly 100 per cent) gave positive reactions to the offending pollens, and only 4 failed to show a skin reaction to the exciting pollens.

If one adds the figures for the combined groups with asthma, urticaria and vasomotor rhinitis, one has a total of 565 patients in whom 3,405 positive skin reactions occurred. Of these, only 940, or 27 per cent, were of clinical importance, but the skin test in pollen disease remains outstanding as an aid in diagnosis.

GENGENBACH, Denver.

TWO CASES OF XERODERMA PIGMENTOSUM OCCURRING IN THE SAME FAMILY. JOHN C. BELISARIO, M. J. Australia **2**:148 (Aug. 3) 1935.

Belisario reports that in a family of eleven children a girl and a boy, aged 14 and 8 years, respectively, had xeroderma pigmentosum. There was no consanguinity. An erythematous squamous dermatitis on the exposed surfaces was observed in the girl at the age of 3 months; the disorder became more noticeable as the child grew older and was exposed to the physical elements. The changes in the skin showed the typical pigmentation, roughness, scaling, telangiectasia and tendency toward malignant changes; photophobia was present. When the child was 3 years old there developed a muscular flexure of the left wrist and a partial loss of function of the left hand and fingers.

The boy showed a similar reaction on the exposed surfaces at the age of 6 months. When he was 2 years old a similar flexural muscular disturbance, together with a weakness of the hand and fingers, as noted in the girl, occurred. The laboratory and roentgen examination of both children gave entirely normal results.

(The point of interest was the development in both patients of palsy of the left wrist, together with the partial loss of function of the hand and fingers. Abstractor.)

BAER, Pittsburgh. [ARCH. DERMAT. & SYPH.]

DIFFUSE SYMMETRICAL SCLERODERMIA. T. PEARSE WILLIAMS, Proc. Roy. Soc. Med. **28**:1325 (Aug.) 1935.

A girl of 4½ years had been well until December 1934, at which time it was noticed that her neck was hard and swollen. A diagnosis of mumps was made at this time. This firm swelling was found to extend and to persist. On examination the skin and subcutaneous tissues of the face, neck, arms, forearms and the lower part of the back and of the abdomen, thighs and legs felt firm and indurated. The Wassermann reaction was negative. The results of examination of the blood and stools are reported.

WILLIAMSON, New Orleans.

DIFFUSE SYMMETRICAL SCLERODERMIA. R. W. B. ELLIS, Proc. Roy. Soc. Med. **28**:1326 (Aug.) 1935.

A case of diffuse symmetrical sclerodermia in a boy, 2 years of age, is described. The results of physical examination, urinalysis, examination of the blood and histologic examination of a portion of skin and subcutaneous fat removed from the right thigh are reported.

WILLIAMSON, New Orleans.

RAPID CURE IN A CASE OF ACRODYNIA BY ACETYLCHOLINE. E. MOURRUT, Bull. Soc. de pédiat. de Paris **32**:377 (June) 1934

A boy, 28 months old, began to lose weight from two to three months previous to examination. He grew rapidly (5 cm. in one month) and showed marked anorexia after a short period of increased appetite. He presented a characteristic picture of acrodynia. He was given injections of 5 cg. of acetylcholine hydrochloride every two days and showed improvement after the second injection. After he had about six injections the treatment was stopped, and a recrudescence of his symptoms then occurred. He was given further injections, and after he had a total of eighteen he was cured. The efficacy of the treatment is attributed to a vasodilator action of the drug.

BENJAMIN, Montreal, Canada.

ERYTHEMA NODOSUM IN THE COURSE OF A PULMONARY ABSCESS. M. NOBÉCOURT and P. DUCAS, Bull. Soc. de pédiat. de Paris **32**:602 (Dec.) 1934.

A pulmonary abscess developed in a girl, 7 years old, after recovery from measles. The tuberculin reaction was at first negative but soon became strongly positive, and at the same time an eruption typical of erythema nodosum appeared on the legs. A roentgenogram of the chest showed an increase of hilar markings as compared with those shown by a previous roentgenogram. This occurred about six weeks after the onset of measles. The child's general condition remained good throughout the course of the disease, and only the roentgenologic evidence of abnormality at the site of the pulmonary abscess and the enlarged hilar shadow persisted. It is possible that the first negative results to the tuberculin tests may have been due to the refractory effect of measles, and the erythema nodosum may have been a manifestation of increased allergy to tuberculin, which sometimes occurs in the presence of a secondary pulmonary infection with pneumococci or streptococci. Inoculation of a guinea-pig with blood from the patient produced no evidence of tuberculosis in the animal, which was killed and examined after three months.

BENJAMIN, Montreal, Canada.

TREATMENT OF ACUTE ECZEMA IN EARLY INFANCY. DONAT LAPONITE, J. de méd. de Paris **55**:782 (Sept. 5) 1935.

In addition to the usual reduction of fat in the diet and the application of salves in the treatment of acute eczema in young infants, the author recommends certain internal medicaments. He believes that some success has attended the use of mild mercurous chloride and also advocates the trial of autohemotherapy. He is most enthusiastic about the use of sodium hyposulfite, which he tries first in small doses of from 1 to 2 cc. This is given by subcutaneous injection, followed, if necessary, by intravenous injection. Four cases are reported.

LESLIE, Evanston, Ill.

TREATMENT OF DISSEMINATED FURUNCULOSIS WITH AUTOGENOUS AND HETEROGENOUS VACCINE. J. M. LÉVINE, Dermat. Ztschr. **71**:85 (April) 1935.

The author has found that autogenous vaccines are much more effective in the treatment of furunculosis than heterogenous vaccines. In cases in which the condition is resistant to treatment local application of Besredka's antivirus is helpful.

TAUSSIG, San Francisco. [ARCH. DERMAT. & SYPH.]

THE SKIN REACTION TO EGG WHITE AND COW'S MILK IN NORMAL INFANTS AND CHILDREN, WITH SPECIAL REFERENCE TO EGG-WHITE IDIOSYNCRASY. NAKAMURA and K. TAKAKI, J. Pediat. (Tokyo), no. 420, May 20, 1935, p. 670.

The skin reaction to egg white is positive in a larger number of normal infants and children, as compared with that to cow's milk (92.1 per cent reactions to egg white and 7.9 per cent reactions to cow's milk). The sensitivity is maximal during

the first year and decreases after the second year. Breast-fed infants show a greater percentage of positive reactions. If the serum of the infant with idiosyncrasy to egg white is mixed with an equal part of a 10 per cent solution of egg white and incubated from two to three hours, the toxicity is greatly increased.

KATO, Chicago.

Surgery and Orthopedics

RESULTS OF SPLENECTOMY IN CHILDHOOD. GROVER C. PENBERTHY and THOMAS B. COOLEY, Ann. Surg. **102**:645 (Oct.) 1935.

The use of splenectomy in the treatment of various conditions is increasing, and since the indications for it have been determined by trial of operation rather than from any previous definite knowledge of the etiology of the various conditions, the authors offer their indications for operation. These they divide into four categories:

1. To put a stop to a perverted, pernicious activity of the spleen (hemolytic icterus, purpura haemorrhagica, erythroblastosis foetalis, sickle cell anemia).

2. To check the progress of pathologic changes in the splenohepatic circulatory system (splenic anemia, splenomegaly with early gastric hemorrhage).

3. To rid the body of the burden of an organ grossly enlarged and rendered useless by disease (erythroblastic anemia, leukemia, Gaucher's disease).

4. To remove a lurking place for certain types of chronic infection (syphilis, malaria, undulant fever, tuberculosis).

The results of twenty-nine splenectomies performed on children are reported.

BANTIN, Omaha.

A BACTERIAL PRINCIPLE IN EXCRETIONS OF SURGICAL MAGGOTS WHICH DESTROYS IMPORTANT ETIOLOGICAL AGENTS OF PYOGENIC INFECTIONS. S. W. SIMMONS, J. Bact. **30**:253 (Sept.) 1935.

Simmons reports that a potent bactericide has been obtained from surgical maggots of the species Lucilia sericata. Bactericidal tests with this substance were conducted with seven species of bacteria of etiologic importance in pyogenic infections. The results showed that exposures of from five to ten minutes were usually sufficient to kill 100 per cent of the organisms in dense suspensions in saline solution and broth. The addition of organic material apparently has less effect on the potency of this material than on that of ordinary disinfectants. The active principle is of a nonviable nature and is not destroyed by autoclaving for twenty minutes at a pressure of 10 pounds (4.5 Kg.). No indication of lysis could be demonstrated by the author, and the thermostability and other reactions of this substance rule out the possibility of a bacteriophage as the active principle. The material was desiccated. In this dry condition it apparently maintains its potency over a longer period than when in aqueous solution. The remarkable bactericidal potency of the excretions against Staphylococcus aureus, hemolytic streptococci and Clostridium Welchii accounts in part for the gratifying results obtained with maggot therapy in infections due to such organisms.

STOESSER, Minneapolis.

SURGICAL JUDGMENT IN OUR APPROACH TO THE ACUTE ABDOMEN. LEGRAND GUERRY, South Carolina M. J. **31**:227 (Dec.) 1935.

A distinction is drawn between an operator and a surgeon. Judgment in operating on the abdomen is considered of primary importance. The author enumerates six "dont's" and elaborates on each: 1. Don't hasten. 2. Don't

delay. 3. Don't use purgatives in the presence of acute conditions of the abdomen. 4. Don't use morphine until the diagnosis is made. 5. Don't be unable to differentiate a contaminated wound from an infected wound. 6. Don't infect the wound.

WESTON JR., Columbia, S. C.

SPLENECTOMY IN THE TREATMENT OF HEMOLYTIC ICTERUS IN CHILDREN. L. BABONNEIX, Gaz. d. hôp. **108**:722 (May 25) 1935.

Two children, aged 10 and 11 years old, respectively, had had recurrent attacks of jaundice since infancy. Enlargement of the spleen and liver, anemia and decreased resistance of the red blood cells were the outstanding symptoms.

Both patients were benefited by splenectomy; the anemia improved, the resistance of the red blood cells returned to practically normal value, and the liver returned to normal size. The period of observation was less than a year.

KAJDI, Baltimore.

RESULTS OF BONE GRAFT IN TUBERCULOSIS OF THE SPINE. M. FRIEDLAND, Rev. d'orthop. **22**:595 (Sept.) 1935.

This is a review of the results obtained in one hundred and sixteen patients under the personal care of the author, compared with the results of conservative treatment. Operative treatment has, in his opinion, shortened the period of treatment six months, on the average, and has produced a higher percentage of "cures."

RYAN, Vancouver, Canada.

SUPRA-EPIPHYSEAL FRACTURES OF THE FOREARM WITH GREAT DISPLACEMENT IN CHILDREN. PIERRE BERTRAND and JEAN JUDET, Rev. d'orthop. **22**:602 (Sept.) 1935.

In supra-epiphyseal fractures there are several obstacles to successful reduction. The distal fragments are short, and it is difficult to mobilize the parts, owing to the interosseous membrane and the radio-ulnar articulation, interposition of the pronator muscle and the displacement of the fragments through the periosteum. Reduction must be accomplished by angulation of the fragments, the thumbs pushing these into position. Alinement is hard to maintain but is best accomplished by an anterior arm gutter, with the forearm in semipronation and the hand flexed to tighten the posterior radio-ulnar ligaments. RYAN, Vancouver, Canada.

Miscellaneous

A STUDY OF A SET OF QUADRUPLETS. A. W. DIDDLE and T. H. BURFORD, Anat. Rec. **61**:281 (Feb. 25) 1935.

Quadruplets occur in 1 of 654,455 labors. The authors studied a set born after a gestation of approximately five and one-half months. This set consisted really of two sets of twins. The two larger infants and the two smaller were alike. The larger twins were dolichocephalic, and the smaller, mesocephalic.

SNELLING, Toronto, Canada.

THE PLASMA-CELL PARTITION OF BLOOD LEAD IN CLINICAL LEAD POISONING. HAROLD BLUMBERG and T. F. MCNAIR SCOTT, Bull. Johns Hopkins Hosp. **56**:305 (June) 1935.

The plasma cell partition of the blood lead was studied in eighteen cases of clinical lead poisoning by spectrographic analyses of the separated fractions from samples of oxalated, citrated and heparinized blood, as well as by analyses of serum and clot.

The results showed that by far the greater part (usually about 90 per cent) of the lead appeared to be carried by the cells or clot. Analyses of control samples of blood, including a sample from a person with hemophilia, indicated that the cell fraction contained at least half, and usually much more, of the trace of non-pathologic blood lead. Washing the cells twice with isotonic saline solution failed to remove appreciable quantities of the lead, thus demonstrating that the lead and the red cells were in comparatively firm combination.

AUTHOR'S SUMMARY.

STRYCHNINE POISONING IN CHILDREN. JOHN R. ROSS and ALLAN BROWN, Canad. M. A. J. **32**:282 (March) 1935.

The authors stress the comparative frequency of strychnine poisoning in children. In the hospitals for sick children in Toronto, from 1919 to 1933, there were thirty-five cases of strychnine poisoning, six of which ended fatally. In twenty-eight cases five of the deaths resulted from ingestion of A. S. B. & C. pills. In most of the deaths the children were between the ages of 1 and 5 years. Statistics were given for the state of New York, where the cases of poisoning were due chiefly to the ingestion of A. S. & B. and A. S. B. & C. pills and Hinckle's cascara.

These facts are brought out in order to advise against the use of strychnine in a formula for such pills.

MOORE, Omaha.

EXPERIMENTAL STUDIES IN ALCOHOLISM: IV. ATTEMPTS TO MODIFY THE CONCENTRATION OF ALCOHOL IN THE BLOOD AFTER INTRAVENOUS ADMINISTRATION OF ALCOHOL. ROBERT FLEMING and DOROTHY REYNOLDS, J. Pharmacol. & Exper. Therap. **54**:236 (June) 1935.

"After intravenous administration the disappearance of alcohol from the blood is the result of five processes: destruction of alcohol in the blood itself, passage into the tissues, elimination by the kidneys, elimination by the lungs and elimination by the gastro-intestinal tract."

The authors had previously found that after intravenous injection of alcohol the alcohol content of the blood of the subjects was relatively constant. They attempted to change this level in twenty of them (mostly heavy drinkers) by various procedures: "egg albumen, milk, cream, olive oil and a saturated solution of magnesium sulfate by mouth; insulin subcutaneously; epinephrine hydrochloride, caffeine sodiobenzoate and physiological salt solution intravenously; carbon dioxide and oxygen via the lungs and diathermy." While diathermy (causing elevation of the body temperature for several hours) resulted in a slight increase in the rate of the disappearance of alcohol from the blood, none of the procedures had any significant effect.

PILCHER, Cleveland.

EVERYDAY PEDIATRICS. E. S. WEGNER, Nebraska M. J. **20**:244 (July) 1935.

Wegner recommends the routine injection of whole blood in all babies born by difficult instrumental delivery. The common cold and its treatment are discussed. Commercial vitamins which are added to common foods are not looked on with favor. Immunization against smallpox, diphtheria and whooping cough is recommended. Immunization against scarlet fever is not included in the list.

HAMILTON, Omaha.

TIREDNESS AS A SYMPTOM IN CHILDHOOD. C. F. STILL, Practitioner **134**:385 (April) 1935.

In this interesting paper Still gives a review of the histories in one hundred consecutive cases in which "tiredness" was a complaint. There were forty-nine girls and fifty-one boys. The youngest patient was 2½ years old; seven patients were under 4 years of age, and thirty-five were from 4 to 7 years old. Still

differentiates tiredness from fatigue in the following terms: "'Fatigue' is a *state* induced in the tissues of the body, particularly in nervous and muscular tissues, by changes, probably chemical, resulting from activity, whereas 'tiredness' is a *sensation* which, though commonly produced by a state of fatigue, seems to exist sometimes apart from any activity produced fatigue."

Tiredness as a symptom in children may have as the underlying cause some defect of general health, such as faulty digestion or constipation, or it may result from absorption of toxins from a focus of infection; anemia and an abnormal condition of the hematopoietic system may be at fault; a faulty school régime may be a factor, or rapid growth during puberty or simple obesity may be the cause.

SAPPINGTON, San Francisco.

FACIAL TUMOUR. R. H. BAILEY, Proc. Roy. Soc. Med. **28**:836 (May) 1935.

A girl, 11 years old, had been shown at a previous meeting of the Section for the Study of Disease in Children as having a zygomatic tumor with (?) papilledema of both disks. No further physical signs developed, and the child was discharged with a diagnosis of "local zygomatic tumour," the condition of the disks having no connection with the tumor. Later she returned for exploratory examination. A small incision was made over the zygomatic process. When the temporal fascia was incised a cystic swelling appeared in which was a small cavity surrounded by some necrotic tissue. The bone appeared normal. The pathologist reported that the tissue suggested chronic inflammation following trauma. A culture was sterile.

WILLIAMSON, New Orleans.

STUDIES ON PHARMACOLOGIC AND PHARMACODYNAMIC REACTIONS OF CHILDHOOD: III. ARSPHENAMINE. LÁSZLÓ VON DOBSZAY and ALAJOS BÁNOS, Arch. f. Kinderh. **104**:25, 1934.

For some time it has been known that infants tolerate two or three times as much arsphenamine per kilogram of body weight as adults or older children. The authors attempted to find the cause for this high tolerance. After intravenous injection of arsphenamine into infants and older children, blood was withdrawn at intervals and tested for its arsphenamine content. It was found that in infants arsphenamine disappears from the blood stream during the half hour after the injection from two to two and one-half times as fast as from the blood of older children.

LEMASTER, Evanston, Ill.

STUDIES ON PHARMACOLOGIC AND PHARMACODYNAMIC REACTIONS OF CHILDHOOD: IV. ARSPHENAMINE. LÁSZLÓ VON DOBSZAY and ALAJOS BÁNOS, Arch. f. Kinderh. **104**:94, 1935.

During a ten day period of study, infants were found to excrete 55 per cent and older children 40 per cent of arsphenamine given intravenously. About one half of the arsenic was excreted in the urine and about one-half in the stool. During the first few days after administration, the excretion of arsenic was mostly through the urine; later excretion was chiefly through the bowel. The excretion of arsenic was greatest during the first few hours after injection. The authors estimated that the excretion of arsenic in infants was practically complete in one month. In infants the excretion of arsenic was about 15 per cent more rapid than in older children.

LEMASTER, Evanston, Ill.

MENTAL AND PHYSICAL DEVELOPMENT OF TWINS. T. BRANDER, Monatschr. f. Kinderh. **61**:414, 1935.

This article is a summary of a much longer one. In the first half Brander submits case histories and photographs showing that examination of the chorion, amnion and placenta does not always determine whether twins are identical or

fraternal. The first pair of identical twins observed by him had a common placenta with two amnions and two chorions. The next pair of obviously fraternal twins had a common placenta, two amnions and only one chorion.

The next part of the article contains a description of a pair of identical twins in which hereditary aphasia occurred in only one. In another set of identical twins cleft palate occurred in only one, and in a third set of identical twins epilepsy occurred in only one. The article concludes with a summary of intelligence tests. A table shows a somewhat lesser variation in the intelligent quotients of the identical twins than in the fraternal group.

In all but one pair of twins there was a definite relationship between the intelligence quotient and the weight at birth, the former being lower when the weight at birth was lower.

GERSTLEY, Chicago.

ANTIDIURETIC EFFECT OF AMINOPYRINE. JOHANNES ULRICH, Monatschr. f. Kinderh. **63**:92, 1935.

Ulrich observed great variation in the urinary output of several of his patients with rheumatism. It was found that this was related to the aminopyrine that they were receiving. A dose of 2 Gm. of this drug daily caused a definite decrease in the amount of urine secreted. This was not due to any renal injury, for there was absolutely no abnormality in the urine. Presumably it was unrelated to perspiration or to changes in the sodium chloride content of the body. Ulrich believes that the suppression of urine resulted from some influence on the thalamic or subthalamic centers.

GERSTLEY, Chicago.

DEPOSIT OF LEAD IN ORGANS. H. HORIE and Y. KOBAYASHI, J. Pediat. (Tokyo), no. 422, July 20, 1935, p. 970.

In seventeen cases of lead poisoning in children the deposit of lead was demonstrated in various organs by the dark-field microscopic method (Timm). The liver showed the largest amount of deposit, and lesser amounts were present in the spleen, kidneys, large and small intestine and gallbladder. The aorta, stomach and thyroid gland contained slight deposits, while the brain, heart, pancreas, adrenals and thymus showed no deposit.

KATO, Chicago.

FATE OF PATIENTS WITH ECLAMPSIA DURING SUBSEQUENT PREGNANCIES AND DELIVERIES. S. KJELLAND-MØRDRE, Norsk. mag. f. lægevidensk. **96**:712 (July) 1935.

The author deals with the much discussed question of the prognosis with respect to subsequent pregnancies and parturitions in patients who have suffered from eclampsia previously.

As to the children, definite information is available in forty-nine cases. Among the forty-nine children, thirty-six were alive and viable, twenty-eight of whom were mature. Two premature but viable children died one and one-half days after birth. Eleven were stillborn; of these, one was mature and seven were viable. Most of the stillborn children were macerated.

The author strongly emphasizes that the interruption of the new pregnancy (abortus provocatus) is not necessary in most of the cases. The question has to be solved individually in each case, and the author mentions a number of factors which he thinks are of significance for the prognosis (e. g., the blood pressure).

TOVERUD, Oslo, Norway.

Society Transactions

NEW YORK PATHOLOGICAL SOCIETY AND NEW YORK ACADEMY OF MEDICINE, SECTION OF PEDIATRICS

Combined Meeting, March 26, 1936

N. Chandler Foot, M.D., *President, New York Pathological Society*

Béla Schick, M.D., *Chairman, New York Academy of Medicine, Section of Pediatrics*

Milton Helpern, M.D., *Secretary, New York Pathological Society*

Alexander T. Martin, M.D., *Secretary, New York Academy of Medicine, Section of Pediatrics*

Splenomegalies of Childhood: Pathologic Aspects. Dr. Paul Klemperer.

The chronic splenomegalies of childhood may be classified according to morphologic pathogenetic principles into six groups: (1) inflammatory, (2) infiltrative, (3) hyperplastic, (4) neoplastic, (5) cystic and (6) circulatory.

Each group has its characteristic histologic criteria. The various splenomegalies which have so far been classified only according to clinical principles—for instance, splenomegaly in cirrhosis, in Cooley's anemia, in hemolytic anemia—can be included in this morphologic pathogenetic classification. The spleen of the patient with so-called Banti's disease or with so-called splenic anemia offers no characteristic histologic criteria. The criteria postulated by Banti can be found in various splenomegalies of various pathogeneses. Continued histologic analysis of any condition clinically suggestive of Banti's disease or of splenic anemia will finally clarify the issue and lead to abandoning this diagnosis of convenience.

Splenomegalies of Childhood: Clinical Aspects. Dr. Rustin McIntosh.

The clinician is under a handicap from the start because of his occasional uncertainty whether a mass occupying the left upper quadrant of the abdomen is the spleen. When the splenomegaly is slight or moderate the organ tends to retain its normal shape and position, so that errors are unlikely; but when enlargement is great other measures in addition to those of routine physical examination must be applied. The most helpful of these in actual experience are excretion urography and fluoroscopy with the barium sulfate enema.

It is well known that in routine examinations the spleen is more frequently felt in children than in adults. In 25 per cent of 151 unselected autopsies it was recorded that the spleen had been clinically palpable. Most of the spleens not felt in routine examination during life were of approximately the average weight for the patient's age, but some among them ranged as high as three times the average weight. In the group of palpable spleens a considerable proportion were of the average size for the patient's age. The largest spleens were those of patients with Gaucher's disease, sickle cell anemia, kala-azar, congenital obliteration of the bile ducts, lymphoid leukemia, congenital hemolytic jaundice, erythroblastosis and congenital syphilis. Palpability of the spleen without conspicuous enlargement must not be assigned too much weight in differential diagnosis of conditions in young patients. Correspondingly, no particular advantage is to be expected from technical tricks which increase the proportion of spleens felt.

Classifications of causes of splenomegaly built up on a histologic basis are generally not satisfactory for clinical use. A grouping of the commoner causes of splenic enlargements according to ages of patients has proved unsatisfactory except as applied to the neonatal period. Splenomegaly in the first month of life is usually related to syphilis, sepsis, congenital malformation of the bile ducts or erythroblastosis; beyond this age, however, the possibilities spread out rapidly. A classification based on the functional behavior of the spleen, while ideal in conception, fails utterly in practice. Approximately seven distinct functions of the spleen have been demonstrated in clinical investigations in man. In any determination of the cause of splenomegaly a judgment based on the results of functional tests becomes obscured, first, because functions do not invariably alter with the change in size; second, because not all functions are simultaneously affected in the same proportion or direction; third, because failing functions of the spleen may be entirely compensated in other parts of the body, and, fourth, because not one of the tests gives results which can be interpreted as representing changes in the spleen alone.

I have attempted to classify the causes of splenomegaly clinically under the following major subdivisions: (1) congenital and familial diseases, (2) mechanical factors, (3) infections, (4) neoplasms, (5) constitutional and nutritional factors, (6) blood diseases not previously included and (7) undetermined influences.

On such a framework any clinician can build a serviceable diagnostic instrument.

In diagnosis, little can be done about the spleen itself except to determine its size. Splenic puncture, staunchly advocated in many clinics, has relatively few advocates in New York. Splenomegaly causes one to place special emphasis on studies of the blood. Besides counting and staining the cellular elements, the usual clinicopathologic measures, one may resort to study of the bone marrow by biopsy or puncture and by use of the roentgen rays; also the rapidity of erythrocyte destruction may be inferred from the output of urobilin in the stools and urine or, less satisfactorily, from the level of bilirubin in the serum. In cases of splenomegaly with associated lymphadenopathy, biopsy of a node may reveal some factor operating in portions of the lymphoid or reticulo-endothelial apparatus outside the spleen and may permit the inference that analogous changes are present in these tissues within the spleen. In suitable cases intensive studies must be directed at the liver. In fact, any promising lead must be followed up, and the diagnostic problem extends into all fields of clinical medicine.

From the therapeutic point of view, the enlarged spleen affords limited avenues of direct attack; it may be observed, irradiated or removed. As a matter of fact, it is in assessing the indications for splenectomy that the functional tests now available render their greatest service to clinical medicine. Aware of my temerity in trespassing on the surgeon's domain, I shall in my paper discuss these indications briefly.

DISCUSSION

DR. MARGIT FREUND: The speakers of the evening have covered the field so completely that it will be difficult to say anything without repeating their statements. However, some of the points may bear repetition.

The clinical diagnosis of splenomegaly is simple in many instances, and exceedingly difficult, almost impossible, in others. With the aid of detailed hematologic investigations one can generally identify the leukemias, constitutional hemolytic jaundice, Cooley's anemia and even Niemann-Pick's disease. The diagnosis may be aided and completed by roentgen examination of the skeleton, as in Cooley's anemia and Gaucher's disease. If such investigative methods are not of help, puncture of the bone marrow may clarify the matter, as in aleukemic leukemia or Gaucher's disease. In kala-azar my co-workers and I have found the Leishman-Donovan bodies. We have carried out this procedure many times within the last years and have never had an accident. It is far less dangerous than splenic puncture.

With these methods of investigation, a considerable number of cases will be clarified. However, in an equal number of cases these laboratory methods are of no avail. These are the cases in which splenomegaly should be called cryptogenetic but in which very often the diagnosis of convenience, "Banti's disease" or "splenic anemia," is adopted. The speakers of the evening have emphasized how unsatisfactory these diagnoses are. We have avoided their use and have tried, when laboratory methods failed, to come to a conclusion by clinical considerations.

A classic example of how the ingenuity of the clinical mind can solve such problems is afforded by the first case of thrombophlebitic splenomegaly seen by Türk, in 1901. This concerned a boy of 10 who had splenomegaly and suffered from frequent hematemesis; the prevailing diagnosis was gastric ulcer, which left the splenomegaly unexplained. Türk noticed the cicatricial condition of the umbilicus and learned that the child had had a severe umbilical infection three months after birth. He correctly concluded that this infection of the navel had propagated into the umbilical vein and caused an occlusion of the portal vein. In the presence of unexplained splenomegaly with hemorrhages from the alimentary tract one must think of occlusion of the portal or of the splenic vein. Wagner and Noble compiled a list of twenty-six cases up to 1933. My associates and I diagnosed such a condition, which was demonstrated at autopsy by Dr. Lederer at the Brooklyn Jewish Hospital, and we have observed a child in whom the histologic changes in the spleen favored this diagnosis. The child is well one and a half years after operation.

The differential diagnosis is most difficult when the condition is confused with cirrhosis of the liver, the occurrence of which in childhood is not exceptional. Slight icterus, which is not rarely present in the latter condition preceding the splenomegaly, may help in the diagnosis. But after employment of all the methods of laboratory and bedside investigation the splenectomy may still bring a surprise.

Such was the case in a girl of 14 whose spleen was referred to by Dr. Klemperer as presenting hyperplastic splenitis. The patient was under our observation for six years. Splenomegaly had been noticed when she was 7½ years of age, a few months before she was admitted to the dispensary of the Mount Sinai Hospital. At the first examination of the blood the hemoglobin was recorded as 70 per cent and the white cell count as 8,000. Gradually there developed moderate anemia, with hemoglobin amounting to 58 per cent, and leukopenia, with a white cell count of 3,400, these paralleling a striking increase in the size of the spleen. The observations well illustrate the fact which Dr. McIntosh pointed out that leukopenia is not characteristic of any particular form of splenomegaly but is the result of the depression of the bone marrow caused by the enlargement of the spleen. Nosebleeds were frequent; once the child had hematemesis. She was much retarded in development. She never had fever or any other evidence of chronic infection. The parents refused puncture of the bone marrow, and therefore Gaucher's disease could not be ruled out. The preoperative diagnosis was Gaucher's disease or thrombosis of the splenic vein. The report of the pathologic laboratory indicated hyperplastic splenitis. Since the operation in November 1934 the child has been well. The hemoglobin is 80 per cent; the white cells number 12,500. She has matured remarkably and has gained 30 pounds (13.6 Kg.). Such a case shows how far physicians still are from the goal of an exact diagnosis of splenomegaly in children.

Dr. David Perla: A great deal has been heard tonight about splenomegaly, and I think there is nothing more to say about it, but it might be interesting to ask why one has a spleen. What is the purpose of the spleen? What is it there for? Is the spleen there only for unusual conditions, and is it interesting only in rare diseases? I have listed a number of functions that I should like to say a few words about. One must not forget, first, that the spleen represents the largest collection of macrophage tissue in the body, that all the elements of the spleen arise from mesenchymal reticulum, the reticular cells; second, that these cells have the capacity under unusual circumstances and also in normal development of

differentiating into a large number of elements. These reticular cells may form free reticular cells, histiocytes or macrophages, or they may form lymphoblastic tissue and lymphocytes, or hemocytoblasts; they may give rise to the hematopoietic tissue and erythroblastic tissue or even to myeloblastic tissue. The mesenchymal tissue represents a precursor of all the macrophage tissue in the body and all the hematopoietic tissue in the body. The third thing to remember is that the spleen is an organ of great sinusoidal capacity, and, on account of its capacity to store blood, is capable of tremendous variations in size. If the members will keep these three thoughts in mind my remarks will be clearer to them.

The spleen serves the purpose of a hematopoietic tissue in animals that have no bone marrow, such as the salamander. In the latter it serves as the site of production of red cells and thrombocytes. In the embryos of man and higher mammals one finds evidence of splenic hematopoiesis, and under unusual circumstances in childhood or during adult life one finds evidence of hematopoiesis in the spleen; again, after severe injury to the bone marrow with the consequent necessity for this type of differentiation of the reticular tissue in the spleen one perceives its ability to form hematopoietic tissue. Dr. Klemperer brought this out very clearly in an article in one of the Libman Anniversary Volumes—this outstanding potentiality of the mesenchymal reticular cells for differentiation into the various elements at any time in life.

The question of the function of the spleen from the point of view of the blood reserve, I think, is relatively unimportant. Barcroft has laid a great deal of weight on this, demonstrating the enlargement of the spleen following hemorrhage. Many other organs have the capacity of expansibility, and I think that an unimportant function of the spleen is this capacity to store blood under unusual circumstances. It means merely that the spleen has an extraordinary capacity for variation in size. It alters many times during a lifetime, and this is due to the elasticity of the tissue of the spleen, which is extremely variable in different animals, and to the tremendous expansibility of the tissue.

There is also the question whether bile pigment is formed in the reticular tissue in the spleen. But I think that by far the most important function of the spleen is to be found in its relation to resistance to infections. There is an impressive amount of evidence from pathologic studies that the spleen is very important in combating acute and chronic infections. This evidence is inferential; there are anatomic changes in the spleen which indicate a powerful stimulation of macrophage tissue, particularly in such diseases as malaria, trypanosomiasis and other protozoan infestations. However, there is considerable experimental evidence that the spleen is related to resistance. The removal of the spleen is in many animals followed by a drop in resistance to acute and chronic infections. In mice and rats the removal of the spleen is followed by marked lowering of resistance to tubercle bacilli, to Bacterium enteritidis, to spirochetes and to trypanosomes. It is interesting, however, that the removal of the spleen is not associated in these animals with a marked drop in resistance to poisons such as histamine; that is, the specific relationship of the spleen to certain types of infection is evident. Even more interesting is the fact that the removal of the spleen is in many species of animals followed by a flaring up of a latent infection. In mice, rats, dogs and other animals there are certain latent infections like bartonella infections. The removal of the spleen converts these latent infections into manifest disease, and associated with this is the occurrence of severe infectious anemia. This is true of bartonella anemia in rats and mice and of a great many diseases in cattle, horses, sheep and the like. Other such diseases are anaplasmosis in sheep and Texas fever in cattle. The finding that the balance in the body between latent infection and manifest disease is controlled to a great extent by the presence of the spleen necessitates a reconsideration of many facts which have accumulated concerning the physiology of the spleen. The belief that there was a relation of the spleen to iron metabolism was based on experimental work of the following nature: The removal of the spleen was in certain animals followed by anemia, and this was interpreted on the

basis that the removal of the spleen had resulted in some impairment of the utilization of the iron and of hemoglobin formation, and consequently the spleen was thought to play some part in iron metabolism and hemoglobin formation, but it is known now that this explanation is not correct.

Of late my associates and I have reported studies on certain strains of rats which were free from all latent infections; we studied the iron metabolism and the copper metabolism, and we found no relation of the spleen to iron metabolism. There is no change in the metabolism of iron in splenectomized animals, but there is a definite alteration in the metabolism of copper; that is, with the removal of the spleen there is an unusual outpouring of copper, followed by the establishment of a negative copper balance, which persists for a considerable time.

I now come to another point, and that is the compensatory mechanism which is set up after the removal of the spleen. This has great bearing clinically on splenectomy. When one removes the spleen one stimulates all the hemoblastic tissue in the body. One can see this in any one of a number of animals. There is intensive stimulation of the hemocytoblasts of the bone marrow; there is development of ectopic foci of formation of lymphocytes in the liver and lungs, to such an extent that the condition of the liver in a splenectomized rat six months after splenectomy closely resembles lymphoid leukemia. Clinically and experimentally we know that for some time following the removal of the spleen there are marked increase, temporarily, in the number of the blood platelets and a marked rise in the leukocytes; so all the derivatives of reticular tissue are stimulated by the removal of the spleen. Once the compensatory mechanism has been established and all these other elements have been stimulated, the rest of the macrophage system takes up the functions of the spleen. The absence of the spleen is no longer detrimental. Its function in natural and acquired resistance is taken over by these elements. The splenectomized animals can no longer be infected manifestly with the diseases to which they were at first subject.

Finally, I should like to say a word about the relation of the spleen to central control. In the last year we have studied the relation of the spleen to the hypophysis, and in a week or so a paper will appear which shows that there is a factor in the anterior lobe of the pituitary gland which exercises a very definite control on splenic tissue. The evidence is based on the fact that removal of the pituitary gland is followed by progressive atrophy of the spleen. This atrophy is much greater than that associated with loss of body weight and is comparable to the atrophy of the adrenal glands or the thyroid gland after hypophysectomy. In the hypophysectomized animal the capacity for splenic tissue to regenerate, as determined after removal of most of the spleen, is lost, so that the stump of the spleen is smaller at the end of a month than it was at first, whereas in the normal animal the spleen regenerates after partial ablation and gradually attains the size of one third or one half of the normal spleen. Extracts of the anterior lobe of the pituitary gland have a marked stimulating effect on the spleen in normal animals, and we have been able to show that this splenic stimulating factor is in the alkaline fraction of the extract of the anterior lobe, that it is quite separate from the thyrotropic and from the adrenotropic substance, and that an extract rich in thyrotropic substance contains no splenotropic substance. Within ten days after the injection of the alkaline extract of the anterior lobe of the pituitary gland the spleen may increase to two or three times the normal size. Not only the spleen enlarges, but also the hemoblastic tissue of the bone marrow and the reticular tissue of the lymph nodes.

Concerning the indications for splenectomy, I should say it is safe to do splenectomy if the spleen has lost its function through tremendous injury, or if a condition is present in which experience has shown that there is an unquestionable beneficial effect, such as follows its removal in hemolytic icterus, hemorrhagic purpura and sometimes Banti's disease. In other conditions the beneficial effect is very transient and is due to the compensatory effects induced by the removal of the spleen. In hemorrhagic purpura there is a tremendous increase in the outpouring of platelets

from the bone marrow. In Gaucher's disease, in a hemorrhagic crisis, the removal of the spleen may modify the hemorrhagic crisis. Otherwise I think the removal of the spleen is contraindicated. Certainly in protozoan infections in the tropics, where removal of the spleen has been tried for cosmetic reasons, because the organ becomes so large, it is invariably followed by a fatal issue.

DR. MAURICE RICHTER: At the annual meeting of the British Medical Association in 1903, the Section of Pathology held a symposium on the pathology of splenic anemia. After listening to several papers, the president of the section summarized the subject by stating that it was quite obvious that the pathology of splenic anemia was wrapped in obscurity. In the last thirty odd years considerably more has come to be known about the pathology of splenic anemia than was known then, because it is now known that splenic anemia does not exist. The term is gradually disappearing from the literature of pathology, and its place has been taken to some extent by the term "Banti's disease." A great deal has been written on the relation between Banti's disease and splenic anemia, and I am glad to hear that all agree that Banti's disease does not exist either. If there were only a few other varieties of splenomegaly that did not exist the question of classification would be simple, but I think there will be for some time a considerable number of types of splenomegaly, the classification of which will be difficult, to say the least. The various criteria for classification that Dr. Klemperer gave are clear, and they are useful for two reasons: In the first place, his classification is one which the pathologist can follow, and, in the second place, the various criteria which he used for placing disease in one or another category are based more or less on objective findings and draw on the imagination only to a minimal extent. I noticed, however, that in the classification of the splenomegalies which Dr. McIntosh gave there are several types which Dr. Klemperer did not mention. Most of these, of course, were omitted only because of lack of time. There are one or two, however, that I rather wish Dr. Klemperer had mentioned in more detail. One is the splenomegaly of sickle cell anemia. I think that this is of interest because sickle cell anemia is one of the few conditions in which the pathologist can make a rather satisfactory diagnosis—to the satisfaction of himself and the clinician. One is accustomed to recognize the pools of blood around the splenic follicles and the sickle shape of the red cell in formaldehyde-fixed preparations as characteristic, whether one regards them as the result of malformation of the splenic sinuses or not.

The other condition which was present in Dr. McIntosh's classification and which was absent in Dr. Klemperer's is the last on the list: the splenomegaly of undetermined origin. That is the bugbear of the pathologist and of the clinician as well, and I think it would be interesting to hear a pathologist try to classify splenomegaly of undetermined origin on the basis of etiology. In the absence of a satisfactory etiologic classification and in the absence of exact knowledge of many of the functions of the spleen, the best one can do is to use purely objective findings. There is, or there is not, congestion; there is, or there is not, hyperplasia of one or the other element of the spleen, and these are practical criteria which can be used.

Regarding other rather minor specific points, I should like to say that at autopsy and at operation I have found it useful to study the spleen in smears, in connection with the usual histologic preparations. If one prepares an emulsion of spleen or makes imprints from the cut surface of the spleen one finds it possible to study the morphology of the cells with the methods that one is accustomed to use for ordinary blood smears, and by these methods certain morphologic details in the cells are brought out more clearly than they are by the section method, thus enabling one at times to identify cell groups and individual cells that are not readily recognized in the ordinary section.

DR. NATHAN ROSENTHAL: The review of the subject has been clear and concise, and the previous speakers have left little for me to discuss.

About twenty-two years ago I saw the first splenectomy for splenomegaly associated with hematemesis, at the Mount Sinai Hospital. This led me to study Banti's disease both in children and in adults, and I have come to the conclusion that this condition cannot be a clinical entity. There are patients with splenomegaly who have gastric hemorrhages, the type of condition described by Osler, and there are other patients with splenomegaly, leukopenia and thrombocytopenia who do not have gastric hemorrhages. These conditions correspond somewhat with that underlying the description by Banti, who never described splenomegaly associated with gastric hemorrhages. In the last group and also in certain others the clinical picture may be dominated by cirrhosis of the liver.

The blood picture does not differentiate all these groups. It shows uniformity: anemia, leukopenia and thrombocytopenia. In still another unusual group, the symptoms may be similar, but the blood picture may not show any changes with respect to the platelets. In the latter group the course following splenectomy is rather stormy, being associated with generalized thromboses. The operation may be followed by persistent or intermittent thrombocythemia. The pathologic examination of the spleen has not helped in differentiating these various types of splenomegaly.

In a study of splenomegaly it is important to keep in mind (1) the various clinical pictures, (2) the blood changes and (3) possible further differentiation by means of sternal puncture. The latter is becoming of increased importance. It is most useful in Gaucher's disease, Niemann-Pick's disease, polycythemia, hemolytic icterus, thrombocythemic splenomegaly and malaria. When thrombocythemia is suspected, a sternal biopsy should be done in order to determine the relative number of megakaryocytes. These are markedly increased in thrombocythemic splenomegaly of the type associated with postoperative thrombosis. (4) An important examination before splenectomy should be that of hepatic function by means of bromsulfalein, the Takata-Ara reaction and a galactose tolerance test (Bauer's). Evidence of hepatic damage contraindicates splenectomy. Splenectomy should not be done before these measures are carefully carried out.

DR. PAUL KLEMPERER: There is one point which is worth reemphasis now that it is agreed that one can diagnose splenomegaly from a purely morphologic standpoint: It is not so easy to make a pathogenetic classification. Nevertheless, this must be the aim. It will be accomplished only with the full cooperation of the clinician and the pathologist, with the aid of the physiologist, who will point the way to new tests and new methods of clinical approach. In this respect I feel that the reference which Dr. Perla made to his work, indicating a relation between the pituitary gland and the spleen, is of great significance. It seems to be significant not only in regard to the problem of splenomegaly but also in regard to diseases of the mesenchyma in general, of which splenomegaly is only a part; for I think one can possibly best regard the spleen as concentrated mesenchyma. Therefore, one can probably study the functions of the mesenchyma in general best in the spleen.

In regard to classification, this was just as troublesome for me as it was for Dr. McIntosh, and I tried many of the classifications given in the literature, and not one was satisfactory either from the purely diagnostic standpoint or from the logical point of view. The difficulty is that these classifications use pathologic and morphologic criteria, on the one hand, and, on the other hand, clinical criteria. Pathologists, however, have to employ chiefly one principle, and I think for the present they have to stick to the morphologic criteria. It is interesting that every one here agrees that Banti's disease and splenic anemia do not denote anything definite. It is then noteworthy that the term "splenic anemia" is still used in the Quarterly Cumulative Index Medicus and even includes Gaucher's disease.

Dr. Richter brought up the question of sickle cell anemia. I did not know whether I should include it or not, for the spleen of the patient with sickle cell anemia is not always enlarged; sometimes it is small; but if one wishes to include it, it belongs in the same group as hemolytic jaundice, with which it has great similarity in the histologic picture.

SOCIETY FOR PEDIATRIC RESEARCH

Annual Meeting, May 5, 1936

Morning Session

CHARLES F. MCKHANN, *President, in the Chair*

ACTION OF MAGNESIUM—EFFECT OF MAGNESIUM ON VASCULAR SPASM. DR. M. I. RUBIN and DR. M. RAPOPORT, Philadelphia.

Since we had demonstrated in a previous experiment that magnesium prevented the contraction of sensitized smooth muscle both in vivo and in vitro, and with the evidence presented by McCollum and his associates, viz., that rats on low magnesium diets showed phenomena suggesting vasoconstriction, it was decided to investigate the effect of diets high in magnesium on vasoconstriction produced in rats by the intramuscular injection of ergotamine tartrate. It has been conclusively demonstrated that ergotamine tartrate produces vasoconstriction, and since hypertension is a manifestation of vasoconstriction, hypertension was used as an index of the presence or absence of vascular spasm.

The normal blood pressure of our rats varied from 78 to 154 mm. of mercury. The average reading was 119, with a standard deviation of ±19. Repeated readings for the same rat showed only a slight fluctuation (about 20 mm. of mercury).

Fifty-four rats were divided into two equal groups. One group was kept on the normal stock diet; the other group was fed the same diet with the addition of 2 per cent magnesium carbonate. This level of magnesium carbonate in the diet did not interfere with normal body growth or normal bone growth. Following the injection of ergotamine tartrate (15 mg. per kilogram of body weight, in three doses at weekly intervals) it was found that the rats on the magnesium diet failed to show hypertension, which was induced in 100 per cent of the rats on the normal stock diet. Removal of the magnesium from the diet was followed by a rise in the blood pressure to hypertensive levels, and, conversely, the addition of magnesium to the diets of the hypertensive rats on the normal diet resulted in a fall of the blood pressure to normal levels.

This experiment suggests the mechanism by which magnesium is effective in lowering the high blood pressure accompanying acute hemorrhagic nephritis.

DISCUSSION

DR. D. C. DARROW, New Haven, Conn.: Did you determine the concentration of magnesium in the serum?

DR. M. I. RUBIN, Philadelphia: No.

DR. L. E. FARR, New York: Did the rats that showed this hypertension for a period of two months or more reveal any renal histologic changes, and did you do urinalysis and find albumin in the urine associated with the hypertension?

DR. M. I. RUBIN, Philadelphia: Until now no urinary or pathologic studies have been made.

OSTEITIS FIBROSA CYSTICA; THE CASE OF A NINE YEAR OLD GIRL WHO ALSO EXHIBITS PRECOCIOUS PUBERTY, MULTIPLE PIGMENTATION OF THE SKIN AND HYPERTHYROIDISM. DR. D. J. MCCUNE, New York.

The patient, a 9 year old girl, is the first child of young healthy Jewish parents. A boy born subsequently is well at 3 years of age. The patient was considered to be normal at birth. Intense jaundice during the first weeks of life led to an erroneous diagnosis of congenital atresia of the biliary passages. Irregularly distributed patches of dark brown pigment appeared in the skin during the second year of life; simultaneously the legs underwent bowing, and the gait

became clumsy. At 2 years of age the patient began to menstruate and has continued to do so from eight to ten times a year; with the advent of the menses the breasts enlarged, and a scant growth of axillary and pubic hair made its appearance. By the end of the fourth year sexual maturity was apparently complete. The concentration of estrogenic substance in the urine has varied between 5 and 95 rat units per liter; gonadotropic substance has been present periodically. From the fourth year onward the patient exhibited evidence of conspicuous hyperthyroidism; the basal metabolic rate has recently attained a level 65 per cent above the normal. Intelligence is unimpaired. Numerous recognized and innumerable unrecognized pathologic fractures of the bones have resulted in progressive deformity. Hematologic examinations have yielded consistently normal findings. The essential roentgen features are: acceleration of maturation of the skeleton, thickening of the skull as in Paget's disease and cystic and productive changes throughout the whole skeleton, which, although bilateral, are more extensive and of greater severity on the right. The values for serum calcium, inorganic phosphorus, nonprotein nitrogen and sodium have been normal on repeated tests. The level of the plasma phosphatase is elevated (from 23 to 37 Bodansky units). Studies of the calcium and the phosphorus balance have revealed a normal retention and a normal partition of the two minerals between the urine and the stools. The microscopic features of the bones are compatible with osteitis fibrosa cystica. Surgical exploration of the neck on one occasion failed to reveal a tumor of the parathyroid bodies. The Hamilton test was negative.

A comprehensive diagnosis has not been made. Information has been obtained concerning 5 identical cases and concerning an equal number of similar cases occurring in boys. The negative evidence of hyperparathyroidism and the anomalies of pigmentation suggest that the skeletal lesions may be of the sort which have been reported in association with typical and atypical examples of von Recklinghausen's neurofibromatosis.

DISCUSSION

DR. C. F. MCKHANN, Boston: I am going to ask Dr. Albright to discuss this paper, by special invitation.

DR. F. ALBRIGHT, Boston: I have seen 4 patients whose cases are pertinent to this discussion.

The first patient was a woman of 23. She had bone cysts, mostly unilateral, suggesting those seen in hyperparathyroidism. The bones which did not have cysts were normal. The values for the blood calcium and the blood phosphorus were normal, and her excretions were normal. We decided that she did not have hyperparathyroidism. A more extensive examination was not made at the time.

The second patient, a woman of 40, came to me also with a diagnosis of hyperparathyroidism. She had several cysts; the rest of her bones were normal. The values for calcium and phosphorus were normal in every way. In going over her history I was surprised to find that she had menstruated at the age of 1 year. Throughout her childhood she had been very precocious. She stopped growing at 10, and the periods continued. She is married and has had children and is perfectly well except for her osseous trouble.

This history was so interesting that I called the first patient back and asked her when her periods had begun. She said at 7 years. The other women in her family had started to menstruate at about 13 or 14.

The third patient, whom I saw last fall, is the one who has been described by Dr. McCune. By that time I thought that there must be some connection between the precocious puberty and the cysts. Then Dr. Crawford, of Illinois, wrote me that he had a patient, a girl of 8 years, with suspected hyperparathyroidism. The values for calcium and phosphorus were not very abnormal, however. One other peculiar fact about his patient, he wrote, was that she began having periods at 3 years. Dr. Patricia Smith then recalled to my memory another young girl with precocious puberty and bone cysts whom I had seen some time ago at the Children's Hospital in Boston. Dr. Allan Butler was kind enough to call

her back, and it was clear that she had the same condition. He will describe her later. All these 4 patients had pigmented nevi like the ones seen in the pictures of Dr. McCune's patient.

One other fact which has recently come to my attention may throw some light on the subject. In a paper in the July 1933 issue of the *Quarterly Journal of Medicine* Snapper reported on a patient who was at first thought to have hyperparathyroidism. At operation no parathyroid tumor was found. Then, after looking over a paper by Kienböck and Meworach on the difficulty of distinguishing xanthomatous bone lesions from osteitis fibrosa, Snapper was led to think that the condition in his patient might be xanthomatosis. By biopsy of bone he was able to prove that this case was one of xanthomatosis and not one of osteitis fibrosa cystica—at least he demonstrated foam cells. His patient also had pigmented nevi and evidence of precocious puberty. She had started to menstruate at the age of 7 years.

Physicians will have to study their cases further from this point of view. The roentgenograms in Snapper's case are exactly like the ones in my cases and like the ones presented. If this disease should be xanthomatosis, there may be a reason for the association between early puberty and the cysts. The metabolism of cholesterol is disturbed in xanthomatosis, and cholesterol is a lipoid and chemically not very different from the estrogenic substances.

There seems to be little question about the syndrome's being an entity. The characteristics are precocious puberty, pigmented nevi and bone cysts.

Dr. A. M. Butler, Boston: We have had a child at the Children's Hospital who also presented a picture similar to that of Dr. McCune's patient. A normal child was born to healthy young Italian parents in June 1930. The child was breast fed for a month. Nothing abnormal was noted until the age of 4½ months, when blood-stained stools were observed by the parents. At 6 months of age the patient was taken to the Boston Dispensary and was found to be a small baby with rachitic rosary, hypotonia, and hypertrophy of the clitoris and of the labia minora and the labia majora. There were brown pigmented areas on the skin of the face, the back of the left leg and the left buttock. There was a bloody, nonclotting vaginal discharge. The Wassermann, tuberculin and Aschheim-Zondek tests were negative. The uterus was not made out to be enlarged. The blood pressure was 90 systolic and 55 diastolic. A roentgenogram of the skull revealed no abnormality. During the following months pigmentation spread to the back of the left shoulder and lower part of back. The patient walked at 14 months.

The precocious sexual development continued, and the child was taken to a physician in March 1933. Roentgenograms taken at this time showed the bones of the skull to be markedly thickened. There were several cystic areas in the bones of the extremities, with absorption around the necks of the femurs, which was particularly marked on the right. The metaphyseal margins were serrated, and there was an irregular flattened collar of new bone around the shaft of the right femur, indicating flowing hyperostosis.

The patient was admitted to the Children's Hospital in December 1933 because of fracture of the left femur incurred as the result of falling from a chair. She was an irritable, mentally retarded, sexually precocious girl of 3½ years. Areas of pigmentation were present as has already been noted. A questionable mass was felt in the upper quadrant, which was thought not to be the spleen. The blood pressure was 100 systolic and 70 diastolic. The red cell count was 5,300,000, with 80 per cent hemoglobin. The white cell count was 9,800, with a normal differential count. A dextrose tolerance test gave a normal curve for the blood sugar. The urine was found to have a specific gravity as high as 1.028, with no albumin, sugar or sediment. The serum calcium content was 9.7 mg. per hundred cubic centimeters; the inorganic phosphorus content, 4.1 mg. per hundred cubic centimeters; the plasma cholesterol content, 114 mg. per hundred cubic centimeters; the serum sodium content, 133 milliequivalents per liter, and the serum chloride content, 100 milliequivalents per liter. The plasma phosphatase

content was 1.5 Kay units. The urine contained no gonadotropic or estrogenic substance. Intravenous pyelography showed normal renal pelves, calices and ureters, with good concentration of the dye. Ventriculo-encephalograms showed somewhat enlarged lateral and third ventricles, with a moderate amount of air over the cortex, indicative of moderate cerebral deficiency. There was no localized distortion. There was an oblique fracture through the left femur about 2 cm. below the greater trochanter. The necks and upper ends of both femurs were somewhat mottled and fibrocystic. There were marked thickening and sclerosis in the cranial and facial bones, which were particularly marked in the occipital, sphenoid, frontal and maxillary bones. The sella turcica appeared normal. The phalanges of the long bones were broader than normal. The bones of the wrist corresponded in development to those of a child of 7 years. The metaphyseal margins were somewhat serrated. There were multiple cystic areas throughout the bones of the arms and legs, which were particularly marked at the upper ends of the femurs.

Though the child was felt to have a polyglandular disturbance probably involving the pituitary gland, the parathyroids, the ovaries and the adrenal glands, an exploratory operation of the adrenal glands was carried out, and a small cyst adjacent to the left ovary was removed. No adrenal tumor could be discovered. On microscopic examination the cyst was seen to be of embryonic mesonephric origin. The child was given six roentgen irradiations of the pituitary region in March, April and May 1934. In December 1934 she fractured the right femur.

She was readmitted to the Children's Hospital in March 1936. Since the last admission she had been having regular menstrual periods every three weeks, using three pads per day for three days. In January 1936 the flow continued steadily for three weeks. Physical examination showed an overdeveloped, mentally retarded child who walked with a waddling gait. Her hearing was not defective, but she talked little, and only a few of her words could be understood. There was markedly precocious sexual development. The pigmentation of the skin had remained as has already been noted. The bones of the head were greatly thickened; the blood pressure was 116 systolic and 66 diastolic. The serum calcium content was 9.7 mg. per hundred cubic centimeters, and the inorganic phosphate content, 3.3 mg per hundred cubic centimeters. The phosphatase content was 0.9 Kay unit, the value for plasma cholesterol, 81 mg. per hundred cubic centimeters; the value for serum protein, 7.1 Gm. per hundred cubic centimeters and the nonprotein nitrogen content, 20 mg. per hundred cubic centimeters. The urea clearance was 116 per cent of normal. The urine contained a trace of Bence-Jones protein but no albumin. There was no gonadotropic or estrogenic substance in the urine. The red cell count of the blood was 4,600,000, with 11 Gm. of hemoglobin per hundred cubic centimeters. The white cells numbered 9,000, with a normal differential count.

X-ray films of the skull showed marked thickening of the cranial vault in the frontal and occipital regions. There was generalized mottling of the vault, and the bone was fuzzy and cotton-like. The facial bones were involved by the same process. There were multiple areas in the ribs that looked like cysts, particularly the axillary borders on both sides. In at least two of these areas on the right there were incomplete fractures. The lungs were essentially clear. The pelvis was markedly distorted, which was evidently the result of softening and cystic degeneration. There were considerable lateral bowing of the upper ends of both femurs and large areas of what appeared to be softening and cystic degeneration, which was most marked in the subtrochanteric regions. The ends of the long bones, such as the radius and the ulna, showed a broad zone of defective calcification adjacent to the metaphyses but extending for some distance from them. There were multiple cystic areas in the shafts of all the long bones. The bones of the hands and feet were involved by the same general process.

Biopsy was not permitted, and a diagnosis has not been agreed on. The differential diagnosis lies between: first, polyglandular dysfunction, primary at the thymus or at the pituitary or pineal gland; second, xanthomatosis, and, third, neurofibromatosis.

Dr. L. E. Holt Jr., Baltimore: I should like to ask whether there were any changes in the periosteum such as have been described in von Recklinghausen's disease.

Dr. D. J. McCune, New York: In answer to Dr. Holt's question concerning the presence in our patient of osseous changes such as have been described in von Recklinghausen's disease, I wish to answer no. My associates and I have had no personal experience with verified conditions of this sort. Our standards of comparison are reproductions of roentgenograms which have been published in the literature. The roentgenographic features presented by this patient do not exactly resemble any reproductions which we have seen. Furthermore, the patient has no tumors of the peripheral nerves. The suggestion as to classification which we have made is based solely on the association of pigmentation of the skin with a bizarre form of osseous dystrophy.

Dr. L. E. Holt Jr., Baltimore: Were there any changes in the eyegrounds?

Dr. D. J. McCune, New York: There were none.

Bacterial Dissociation in the Dysentery Group as Related to Clinical Infection. Dr. P. Dooley, New York.

As a part of an epidemiologic study of bacillary dysentery, the colonial forms of the strains obtained in primary isolations from 42 persons have been observed at the time of the original isolation and of subsequent isolations and have been followed under standard laboratory conditions in comparison with twenty-seven historical strains of the dysentery group similarly followed.

DISCUSSION

Dr. J. D. Trask, New Haven, Conn.: Dr. Dooley makes me wonder whether or not studies similar to his can be applied to rheumatic fever and hemorrhagic nephritis by investigators interested in the relation of hemolytic streptococci to these diseases. I think that this would be hard to do, because dissociation among streptococci is poorly understood.

Dr. H. W. Scherp, Philadelphia: I should like to ask Dr. Dooley whether he has any information about the occurrence or nature of specific substances in these organisms, analogous to the polysaccharides of the pneumococcus.

Dr. P. Dooley, New York: In this particular study my associates and I were dealing with whole organisms and aggregate populations and not with any fractions.

Effect of Protein in the Diet on the Urea Clearance of Children with Nephrosis. Dr. L. E. Farr, New York.

The effect of protein in the diet on the urea clearance of 4 nephrotic children all aged 4 years was observed. The children had been under observation for several months before these studies were begun, and all of them showed consistent and constant elevation of the urea clearance, averaging about 175 per cent of the normal. During the period of observation the intake of calories and of sodium chloride was kept constant. Fat and carbohydrate were varied inversely with protein to maintain a constant caloric intake. The changes in urea clearance were observed over seven successive periods. For each period several days were allowed for the dietary change to produce its effect on renal function; then the urea clearance was observed on two successive days. The tests for urea clearance were carried out over two consecutive twelve hour periods instead of the usual one hour period. The children were well throughout the period and took the diet without difficulty.

The results were as follows: The urea clearance was found to vary markedly with the intake of protein. Intakes of protein of 0.5, 1, 2, 3 and 4 Gm. per kilogram of body weight per day were accompanied by average urea clearances of 73, 88, 178, 184 and 216 per cent of the mean normal, respectively. The creatinine clearance showed variations similar to those of the urea clearance. The administration, during periods of a low intake of protein, of urea sufficient to produce

outputs of urea like those observed during periods of a high intake of protein caused a relatively slight increase in the urea clearance.

It appears that the stimulus of renal function by high protein diets was due to products other than urea. The effect of the intake of protein on the urea clearance in our patients was much greater in magnitude than similar effects observed in adult human subjects, either normal or with renal disease. It remains to be ascertained by control observations on normal children whether the noted lability of the clearances is common to young children or whether in our patients it was due to the combined effect of early age and the nephrotic syndrome.

DISCUSSION

Dr. J. D. Lyttle, New York: It is my recollection that in chronic nephrosis the intake of chloride has a definite relation to the urea clearance. In the first chart it seemed to me that the fall in the urea clearance coincided with a period of restricted intake of sodium chloride. I do not see how the chloride metabolism can be disregarded in interpreting the urea clearance.

Dr. A. M. Butler, Boston: I think that Dr. Lyttle's comment applies only to patients with nephritis who have markedly diminished renal function. Dr. Farr's patients do not fall into that group, and probably restriction of chloride would not affect the urea clearance.

Dr. L. E. Farr, New York: The first slide was probably not so clear as it might have been. The intake of chloride was kept constant throughout the entire period; there was no diminution in the intake of chloride. The only variation in the diet was in the protein content. The percentages of carbohydrate and fat were varied inversely with the protein content to keep the caloric intake constant, but there was no change in the intake of sodium chloride.

Prevalence of Reduced Serum Proteins in a Southern Clinic. Dr. Katharine Dodd and Dr. Ann S. Minot, Nashville, Tenn.

Generalized edema of neither cardiac nor renal origin occurs fairly frequently among the poorer children in Tennessee. There is always a marked decrease of the serum protein content, especially of the albumin fraction. In this locality the underlying cause of the low serum protein content is usually a diet which is grossly inadequate in total calories and in protein, either because of ignorance on the part of the parents or because of long-continued economic stress. Determinations of the serum protein content were made on normal well nourished children in order to establish normal levels for children of various ages. The general level of the serum albumin in 500 children in our group in the clinic, even in the absence of acute or chronic illness, is somewhat below that of the normal group. The serum albumin content of children with acute or chronic infection rarely reaches the normal average except in the presence of dehydration. We believe that the level of serum albumin is a useful index of the state of nutrition of children.

DISCUSSION

Dr. A. A. Weech, New York: These observations which Dr. Dodd has presented, together with similar findings for adults which Dr. Youmans has reported from the same clinic, strongly intimate that this form of deficiency is more common in Tennessee than in other parts of our country. To the best of my knowledge, however, no similarly comprehensive series of measurements has been made in other places, and it is necessary to admit that mild protein deficiency may be generally more common than has been thought.

I should like to ask Dr. Dodd whether she has made any analyses of edema fluid for determination of the protein content. The currently accepted theory of the pathogenesis of this form of edema postulates that the impermeability of the capillary wall for protein is not altered. Direct analysis of edema fluid provides the only means for checking the postulate, and, unfortunately, the number of analyses recorded in the literature is small.

Dr. D. C. Darrow, New Haven: I should like to know whether Dr. Dodd has any evidence concerning the immediate effect of infection in lowering the serum

albumin content. I have had the impression that infection rather rapidly reduces the serum albumin content when one cannot be sure that the infection has led to sufficient starvation to induce a nutritional disturbance.

DR. L. E. FARR, New York: I should like to ask Dr. Dodd whether she has correlated the level of the serum albumin with the appearance of edema, in the absence of infection or other causes for edema in her patients. In our series of nephrotic children my associates and I have found a close correlation between the degree of edema and the level of the plasma albumin.

DR. KATHARINE DODD, Nashville, Tenn.: In reply to Dr. Weech's question, we have not done any analyses on edema fluid.

We have no figures for children before and after infection, so we cannot answer Dr. Darrow's question. We have the impression that at least certain types of infection must lower the value for serum protein rapidly and that the serum albumin content is lower in children with infection than in those with no infection.

As far as the level of albumin at which edema occurs is concerned, I do not believe that there is any exact level. Too many other factors come into play, such as the intake of fluid and of sodium chloride. Although these children recover from the edema on a good diet, there is at times little change in the serum protein content when the edema first disappears. There are children without edema in whom the serum albumin content is just as low as in those with edema, but on the whole the albumin content tends to be a great deal lower in the children with edema than in the other children.

OCCURRENCE OF ESSENTIAL HYPERTENSION IN RHEUMATIC INFECTIONS. DR. HELEN B. TAUSSIG and DR. M. S. HECHT, Baltimore.

This study was undertaken because we observed high blood pressure in many children suffering from rheumatic fever and chorea and found that of these, 2 children had shown essential hypertension under observation. By essential hypertension is meant a permanently elevated blood pressure, with a diastolic pressure of 90 or more, for which no cause is found, i. e., no cardiac condition, no glandular disturbance, no evidence of acute or chronic nephritis, no evidence of arteriolar sclerosis and no impairment of renal function.

Only children for whom four or more determinations of the blood pressure had been recorded were included in the study. Furthermore, all patients showing any of the recognized factors which alter blood pressure were excluded. Five hundred cases of rheumatic fever and chorea were analyzed. Two hundred and seventy-three of these patients showed a normal blood pressure. Fifty-three of them showed definite and certain evidence of hypertension at one time or another. The remaining 174 at times showed an elevated blood pressure; however, as all possible complicating factors had not been excluded, these cases were classed as questionable, and the patients were not considered to show true hypertension.

The 53 children who did show genuine hypertension were divided as follows: 4 appeared to have essential hypertension; 10 others showed periods of high blood pressure but have not been followed for a sufficient length of time to enable us to determine whether or not it will be permanent. The remaining 39 showed transient hypertension during or immediately after an acute rheumatic episode. In 5 the hypertension occurred in association with chorea, in 11 in association with chorea and rheumatic fever and in 23 in association with acute rheumatic fever. Each hypertensive patient in whom the blood pressure had not returned to normal was subjected to a thorough renal investigation; i. e., in addition to the routine urinalysis a determination of the nonprotein nitrogen content and of the fractional excretion of phenolsulfonphthalein were made, and an intravenous pyelogram was taken. None of the patients showed any evidence of renal impairment, and only 2 exhibited a slight abnormality in the pyelogram (one showed a horseshoe kidney, and the other, a slightly dilated pelvis). All showed normal eyegrounds and a normal blood pressure in the lower extremities. In short, no other cause than rheumatic fever or chorea was found to explain the hypertension.

The relation between exertion and hypertension is discussed. If the exertion of the trip to the dispensary is sufficient to cause an elevation of the blood pressure an indication exists for the limitation of the child's activity.

Whether this phenomenon of hypertension is a specific response to rheumatic fever or a response shown in a group of diseases of which rheumatic fever is one is not known. It is possible that the rheumatic infection merely makes manifest an inherent underlying tendency to hypertension. It is also conceivable that the repeated recording of the blood pressure in children merely brings to light a large number of cases of early hypertension and that the rheumatic infection is incidental.

It is concluded that hypertension does occur in children and that high blood pressure readings in children deserve careful investigation. Furthermore, the hypertension seen so frequently during and immediately following rheumatic episodes is probably in some way related to an active rheumatic infection.

DISCUSSION

DR. MAY G. WILSON, New York: It would seem evident from Dr. Taussig's findings that more attention should be paid to routine blood pressure readings. I think that all the members have been impressed with the marked fluctuations in the blood pressure in children and for this reason may have overlooked many early cases of essential hypertension. It would be interesting to follow the blood pressure of a series of rheumatic patients who are under continuous observation over a period of years to determine whether there is any relationship between rheumatic fever and essential hypertension. Of course, it would also be necessary to follow an adequate control group, including those with other infections, before the finding of an elevated pressure, particularly a diastolic pressure of 90, can be considered significant.

DR. A. M. BUTLER, Boston: I could not help but notice from the charts that the great majority of patients fell within the age group of from 12 to 16 years. In that age group, particularly in girls, there tends to be an elevation in the blood pressure, and I wonder whether Dr. Taussig has observed a series of normal persons falling within that particular age range to provide a normal standard against which to appraise the significance of her data.

DR. J. D. LYTTLE, New York: I should like to ask Dr. Taussig whether the family history in these children with essential hypertension reveals any unusual incidence of cardiac, vascular or renal disease and whether the blood pressure of the parents of these children was taken.

DR. HELEN B. TAUSSIG, Baltimore: In answer to Dr. Wilson's question concerning control studies, we fully appreciate the need of, and we have planned to make, control studies, not only to determine the normal blood pressure at the various ages but especially to determine the extent of the fluctuation in the blood pressure level which occurs in normal children.

In answer to Dr. Butler's question concerning the rise in the blood pressure at puberty, it is true that a sharp rise occurs at that age. However, we do not believe that a diastolic pressure of 90 is normal even at puberty. So far as we know, no group of patients who show marked elevation of the blood pressure at or immediately after puberty, such as Alvarez reported, have been followed for a sufficient length of time to ascertain whether or not they showed essential hypertension at 40 years of age.

In this connection the work of Levine and Fulton concerning the frequency of hypertension in patients with mitral stenosis is of interest. They reported that 50 per cent of the patients with mitral stenosis over 40 years of age showed essential hypertension. It is today merely a matter of speculation whether these children who show a tendency to hypertension represent the group who will show hypertension at 40. In some cases, however, essential hypertension has developed under observation.

In answer to Dr. Lyttle's question concerning studies of the family, we are planning to undertake such studies and hope to be able to report on this another year.

EFFECT OF HIGH PROTEIN DIET ON DEHYDRATION. DR. H. L. HODES, Baltimore.

An attempt was made to evaluate the effect of a diet of high protein content on the ability of rats to withstand reduction of their intake of water. One group of rats was fed a diet high in protein, another a diet high in carbohydrate and a third a diet high in fat. The three diets were identical in vitamin and mineral content. After a control period of food and water ad libitum the rats were subjected to two periods of reduced intake of water. After this their drinking water was removed completely. All through the experiment food was permitted as desired. During the control and experimental period the caloric intake and the total intake of water per hundred grams of body weight were nearly the same in all three groups.

It was found that, on the average, the rats on the high carbohydrate diet survived five days after their drinking water had been entirely removed, while the rats on the diet high in fat survived about four days without drinking water. The rats fed the high protein diet lived less than one day after their drinking water had been withdrawn.

During the experiment the rats on the high protein diet were supplied by their food with three times as much nitrogen as the rats on the high fat diet and the rats on the high carbohydrate diet. The influence of this factor was tested in the following way: The three diets previously described were again employed. However, urea was now added to the high fat diet and to the high carbohydrate diet. The quantity of urea added was equal to the urea furnished by the excess protein in the high protein diet. The regimen of reduction of water was carried out exactly as before. In this experiment the rats fed the high carbohydrate diet and those fed the high fat diet did not survive the withdrawal of water any longer than the rats on the high protein diet. All three groups died within one day after the complete removal of their drinking water.

The findings may be summarized as follows: 1. When rats are fed diets differing only in their carbohydrate, fat and protein contents the animals on the diet high in protein do not withstand restriction of their intake of water so well as those on a high carbohydrate diet or those on a high fat diet. 2. The greater quantity of urea furnished by the high protein diet seems to play a major rôle in the greater susceptibility to reduction of water shown by rats fed on this diet.

DISCUSSION

DR. S. Z. LEVINE, New York: Was the body temperature of the rats measured?

DR. L. E. HOLT JR., Baltimore: I wonder whether Dr. Hodes would care to comment on the fact that the rats fed on the high fat diet gained very poorly.

DR. H. L. HODES, Baltimore: In answer to Dr. Levine's question, my associates and I did not attempt to determine the body temperature of the rats.

The poor condition of the rats fed the high fat diet was due to prolonged heating of the lard which was used in the diet.

Later experiments showed that rats grew normally and remained healthy when they were fed diets containing lard which had been dried in an oven at 105 C. for twenty-four hours. However, when the lard was kept at 105 C. for four days or longer the rats on the high fat diet were affected. Their daily gain in weight dropped sharply; they seemed listless, and their fur became thin. On the other hand, the rats fed the high carbohydrate diet and those fed the high protein diet were unaffected when the lard in their diets was similarly overheated. We believe, therefore, that prolonged heating renders the lard toxic when it is fed at a high level.

Further evidence of the toxicity of the heated lard was obtained in the following way: Rats were placed on a diet which was exactly like the high fat diet previously described except that the lard was kept at 105 C. for only twenty-four hours. In this case the rats grew perfectly well. After ten days their diet was replaced by one which was identical in every way with the previous diet except that it contained lard which had been heated for four days. There was an immediate

drop in the daily gain in weight; the animals became listless, and their fur grew thin. After ten days the diet of overheated lard was removed, and the rats were once again fed the diet which contained lard heated only twenty-four hours. The rats at once began to gain rapidly, and in a short time they looked healthy again.

Dr. S. Z. Levine, New York: May I comment in regard to the reason for my question?

I do not believe that changes in the body temperature would necessarily have any relation to the external environment, but it is possible that in the presence of an excess amount of nitrogenous waste products in the circulation the urinary excretion might have demanded an increased output of water, with a consequent reduction of available moisture for vaporization from the skin. If the rats died with a high temperature, I think that this mechanism might have accounted for the rapid deaths, especially in the case of the rats fed protein or those fed urea.

Dr. H. L. Hodes, Baltimore: I think that one can tell by feeling the rats. The rats which we studied were not warmer than usual. Their skin was colder.

Lipids of the Blood Plasma in the Neonatal Period. Dr. M. J. E. Senn and Miss Helen McNamara, New York.

This article will be published in full in a later issue of the American Journal of Diseases of Children.

Use of Purified Poliomyelitis Virus in Active Immunization. Dr. H. W. Scherp and Dr. I. J. Wolman, Philadelphia.

Three technics have been investigated for their utility as means of purifying the poliomyelitis virus: (1) methods for fractionation of protein, (2) extraction with ether and (3) adsorption and elution methods. All these were applied to 10 per cent saline extracts of virus-containing monkey spinal cords. The principal impurities were extraneous protein, nonprotein nitrogenous extractives and suspended matter (lipoid and tissue particles).

Salting out experiments with ammonium sulfate have confirmed the findings of other workers that the virus is associated with the pseudoglobulin fraction. Various preparations of this fraction contained from 10 to 20 per cent of the amount of protein in the original material. The fractionation was often rendered indistinct by the presence of nerve tissue lipoid. Also, the time required was undesirably long.

When saline extracts of spinal cord were acidified to p_H 4.6, about 75 per cent of the protein present was precipitated iso-electrically. The virus was equally distributed between the precipitate and the supernatant fluid and was not diminished in potency.

When saline extract of cord was shaken out with purified ether and the mixture was centrifugated, a layer of emulsion formed at the interface of the water and the ether. The aqueous layer was completely clarified, and its protein content was diminished by 30 per cent. The virus was largely inactivated.

Adsorption and elution methods have been the most satisfactory. The following agents have been used: (1) the acid, negatively charged aluminum hydroxide gel of Brewer, (2) the alkaline aluminum hydroxide gel of Willstaetter, type C, and (3) kaolin. The action of these adsorbents was similar. They tended to adsorb all protein, virus and suspended matter, leaving the nonprotein nitrogenous extractives. The Brewer gel was irregularly successful in freeing virus preparations of suspended matter, with slight loss of virus by adsorption. The best results were obtained by using an excess of the adsorbent and then liberating the virus by eluting with di-sodium hydrogen phosphate in the case of the aluminum hydroxide gels and with one-hundreth normal ammonium hydroxide for kaolin. Clear, colorless eluates were obtained, with the virus unaltered in potency

and accompanied only by extraneous protein. The protein content was from 20 to 40 per cent that of the original material, or from 6 to 12 mg. per gram of wet weight of spinal cord used. No evidence has been found that the virus is adsorbed or eluted preferentially to the bulk of the protein.

The inactivation of the virus by solution of formaldehyde at —4 C. was investigated. Inactivation proceeded more readily and consistently the less extraneous material there was present. Exposure of virus as extracts of cord or eluates to 0.2 per cent solution of formaldehyde for forty-eight hours left the preparation noninfective for the monkey. Uncentrifugated suspensions of cord exposed similarly to 0.3 per cent solution of formaldehyde retained their infectivity.

The formaldehydized virus has been used for active immunization of monkeys. The results to date indicate that multiple subcutaneous injections of large amounts render a majority of the vaccinated animals resistant to the active virus when instilled intranasally and a minority resistant to the virus when inoculated intracerebrally. Vaccination with the formaldehydized virus appeared to be more efficacious, as well as less dangerous, than vaccination with living virus.

DISCUSSION

Dr. J. D. Trask, New Haven, Conn.: I can corroborate the finding that formaldehydized virus is not always inactive. In addition, Dr. Paul and I have noticed that different strains of the virus vary considerably in the amount of formaldehyde that they withstand. We have been studying six strains of virus. One of the strains from the 1934 epidemic withstood formaldehydization very well. It was active after twenty-four hours' exposure to 0.2 per cent solution of formaldehyde. A 1931 strain also stood the same amount of exposure to solution of formaldehyde on one occasion, whereas the other strains were killed by that amount.

Dr. F. F. Schwentker, Baltimore: As long as one uses emulsions of cord tissue as the source of virus for immunization against poliomyelitis or against any other disease it would seem that purification is going to be an essential, or at least a desirable, feature. The work of Dr. Rivers and his associates has shown that when emulsions of brain tissue are injected into monkeys, demyelinating lesions may occur which are similar to those that sometimes follow vaccination against rabies or follow some of the acute communicable diseases.

The present indication is that the factor in the brain tissue which causes demyelinization is a lipoid. It would therefore seem that purification against the fats is just as important as purification against a protein.

Dr. H. W. Scherp, Philadelphia: We are aware, as Dr. Trask has pointed out, of the difficulties that one encounters when inactivating poliomyelitis virus with solution of formaldehyde. The use of formaldehydized poliomyelitis virus for active immunization is in rather bad repute at present.

We have used one strain throughout, the Philadelphia 1932 strain, in an attempt to obtain consistent results. So far as our results are concerned, we have been able to protect a majority of the vaccinated animals against poliomyelitis, using formaldehydized virus. When active virus was used there was a considerable incidence of poliomyelitis in the animals during the course of immunization. Strangely enough, the remainder, after vaccination, proved not to be immune to the virus when this was instilled nasally.

The question may, of course, arise as to the efficacy of the intranasal test. We can only say that our controls have shown consistently positive results.

Afternoon Session

Variations in Ossification Pattern Observed During First Five Years. Dr. H. C. Stuart and Miss Vernette Vickers, Boston.

This is a preliminary report of the roentgenographic findings in a study of 77 normal boys and their relation to health and development. Attention has been

given to the range of variation in the time of appearance of each center, and lantern slides show tables and charts of these ranges. X-ray films of 2 children at successive ages show the differences between the most retarded and the most advanced ossification pattern in the series. This range is as great, although slightly more advanced in point of age, as in reported groups of less carefully selected children. The consistency of order of rank of individual boys at successive ages is great, and the order of ossification of bone centers and epiphyses is regular. Some centers tend to appear at nearly the average in all boys while others appear at such widely different ages as to make the average meaningless.

This study has been primarily concerned with the differences which exist between children with the most retarded ossification patterns and those with the most advanced ossification patterns in relation to mental and physical development and to health and environmental experiences. A practical objective has been to evaluate the roentgenogram of the wrist and hand as an adjunct to health examinations and to discover the significance, if any, of observed variations.

Comparison of the 4 subjects with the most retarded ossification patterns with the 4 subjects with the most advanced ossification patterns revealed no sharply differentiated types and no evidence of hypothyroidism in those in whom ossification was retarded. A composite curve for height for the subjects with a retarded ossification pattern fell constantly below that for the subjects with an advanced ossification pattern, but the curves for weight were not characteristically different. In other physical attributes the boys with a retarded ossification pattern tended to be less adequate than those with an advanced ossification pattern and showed slower closure of the fontanels, although not slower eruption of teeth. The subjects with a retarded ossification pattern presented on the whole more unsatisfactory health histories than those with an advanced ossification process, and delay in progress of ossification times seemed to be caused by major illness. Of the 4 boys most retarded in point of ossification, 2 were average mentally and 2 were consistently retarded, whereas all the 4 boys with the advanced ossification patterns were definitely above the average in mental ratings. There was, however, no regularity about most of the differences, certain boys with an advanced ossification pattern being definitely inadequate in some respects and certain boys with a retarded ossification pattern receiving excellent ratings. Also, severe illness did not always retard the progress of ossification, at times even appearing to advance it. The lines of interrupted growth found in the shafts of the long bones appeared to be more consistent indicators of previous ill health than ossification of centers.

X-ray films of the extremities in this series seemed to contribute more useful information by revealing differences in osseous structure at the zones of growth than by revealing the pattern of ossification. The presence or absence of individual centers at a given time has far more significance if the relative advancement at a previous time is known. Changes in order of rank or alteration in the rate of progress are of far more interest than deviations from the customary findings for age and sex. In this respect some centers are far more significant than others.

DISCUSSION

DR. A. A. WEECH, New York: Can the chronological age of a child be predicted more accurately from the findings in a number of joints than from the findings in a single joint?

DR. H. C. STUART, Boston: There are certain ages at which it is undoubtedly true that the study of other centers besides those in the hand and wrist will add to the understanding of a child's developmental age. There are relatively long periods during which nothing particular happens in the wrist or at least there is nothing to be guided by but changes in size or shape. The study of other centers during these periods will be helpful. We have x-ray films of all the centers in the body taken at each examination in this series but have considered only the hand and wrist at this time. In general, however, if the ossification of the hand

and wrist is advanced, that of the foot and ankle is also advanced. A child usually shows advancement or retardation or an average median condition in regard to ossification in all the bones.

If one knows early in life that a child has an advanced ossification pattern and compares him later with children with an advanced ossification pattern the study of the centers in the different parts of the body may be of help in determining whether his progress has been satisfactory. If, however, one does not know what his previous pattern was, I do not believe that the study of all the skeletal centers will prove much more helpful than the study of appropriately selected areas.

Basal Metabolism and Heat of Vaporization of Premature Infants. Dr. H. H. Gordon and Dr. S. Z. Levine, New York.

This article will be published in full in a later issue of the American Journal of Diseases of Children.

Titration of Human Passive-Transfer Antibody by Neutralization. Dr. V. W. Lippard and Dr. W. M. Schmidt, New York.

Titration of the passive-transfer antibody of human hypersensitivity by specific neutralization was suggested by Woringer. The purpose of this investigation was to develop and to define more clearly a neutralization method so that it might be applied to studies of clinical hypersensitivity associated with a variety of antigens.

The method described is based on the determination of the amount of antigen necessary to neutralize the available antibody in a given amount of serum. The procedure involves the mixing of various dilutions of antigen with constant amounts of serum in vitro, intradermal injection of the resultant mixtures and subsequent intramuscular injection of antigen. Following intramuscular injection, reactions appear at cutaneous areas where incompletely neutralized serum was injected. The titration level is based on the smallest amount of antigen which inhibits sensitization.

For standardization of antigens the method of concentration of the total nitrogen is adopted. One unit of passive-transfer antibody is defined as the amount neutralized by the quantity of antigen which contains 0.00001 mg. of total nitrogen. The titer of a serum is recorded as the number of units of antibody per cubic centimeter of the standard antigen-antibody mixture.

The amount of antigen which must be injected intramuscularly in order to produce reactions at sensitized cutaneous areas was determined experimentally. There is no evidence to indicate that recipients are sensitized by these injections.

No alteration in titer was noted in mixtures stored for from two to six months. Nonspecific neutralization was not observed in titration mixtures.

The technic described was found applicable to the study of serum obtained from patients with several allergic disorders. Furthermore, equally good results were obtained in titrating with a variety of antigens.

Composition of the Fetal Skeleton. Dr. W. W. Swanson and Miss Vivian Iob, Chicago.

In a recent paper Toverud and Toverud showed that the calcium and the phosphorus content of bone taken from premature infants ranging in age from 30 to 38 weeks was constant. In the present study a similar and more comprehensive investigation was made of the composition of the long bones from fetuses from 16 to 40 weeks of age. From tables giving the concentrations not only of calcium and of phosphorus but also of sodium, potassium, magnesium, chlorine and sulfur of various long bones removed from the fetuses it is observed that during the period in which rapid skeletal growth of the fetus takes place there occur: (1) a decrease in the water content of the bone, (2) a decrease in the concentration of magnesium and (3) a less marked decrease in the concentration of chlorine and of sodium. Figures obtained from analysis of the cartilage of

these bones show a similar decrease in the water and the magnesium content. In cartilage the concentration of phosphorus exceeds that of calcium; however, 77 per cent of the total phosphorus of cartilage is found to be in combination with organic lipoid, in contrast to the 1 per cent of the total phosphorus of bone extractable by lipoid solvents.

DISCUSSION

DR. R. MCINTOSH, New York: Has it been possible to explain the variations among the patients in this series on the basis of the diet of the mother, with particular reference to the intake of minerals and of vitamins?

DR. D. C. DARROW, New Haven, Conn.: I am interested particularly in the data which show that the amount of sodium in bone exceeds that which can be accounted for by the cellular fluid. Marble bones as well as normal bones contain sodium which is not dissolved in extracellular fluid. Also, as has been known for a number of years, sodium is present in cartilage in greater concentration than in bone.

DR. W. W. SWANSON, Chicago: In regard to Dr. McIntosh's question, we have had no opportunity to study the mothers from whom we obtained the fetuses for our analyses. We have, however, carried out experiments on pregnant rats in which we increased the intake of vitamin D and kept the animals on a diet moderately high in calcium and phosphorus. This regimen did increase the calcium and the phosphorus content of the offspring, as determined by analysis of the body as a whole.

Further, Toverud and Toverud have shown that the skeleton of the premature infant has a lower calcium and a lower phosphorus content when the diet of the pregnant mother is deficient.

RELATIONSHIP BETWEEN VAPOR PRESSURE AND THE SOLUTES OF SERUM. DR. R. W. CULBERT and DR. D. J. MCCUNE, New York.

In a group of serums determinations of the following were made on each sample: the vapor pressure, the total amount of base, the nonprotein nitrogen content, the bicarbonate content, the chloride content and the protein content. The data of the results were analyzed by the method of partial correlation. The finding of a high coefficient of multiple correlation among the vapor pressure, the nonprotein nitrogen content and either the amount of total base or the sum of three anions has made it possible to derive regression equations with which the vapor pressure can be predicted from several of the solutes of serum. The consistency of the results and the nature of the relationships in the equations support the contention of A. V. Hill that the vapor pressure of serum is a measure of its osmotic pressure.

DISCUSSION

DR. A. A. WEECH, New York: The most fascinating feature to me in this work that Dr. Culbert has presented is the possibility of predicting the osmotic pressure of serum without any knowledge of its protein content. The prediction by the formula which omits protein is approximately as accurate as that by the formula which includes it. The use of a pipet to measure the size of the sample in analysis of the nonprotein nitrogen content and of the base content is admittedly an inexact substitute for actually weighing all the samples and determining their water content. In this case, however, the error of the pipet measurement has such a size and direction that it compensates almost exactly for the error introduced by omitting the protein content in the regression equation. I do not believe that this result could have been guessed in advance.

DR. D. C. DARROW, New Haven, Conn.: I made similar calculations by assuming values for the activity of the ions, with much the same results, although the formula was not nearly so well worked out mathematically. It seems to me that with Dr. Culbert's and Dr. McCune's ingenuity the inclusion of a conductivity measurement along with measurement of vapor tension should yield a much more accurate formula for predicting the total amount of base.

ACTIVE IMMUNIZATION WITH THE VIRUSES OF HUMAN AND SWINE INFLUENZA. DR. ALICE CHENOWETH, DR. A. D. WALTZ, DR. J. STOKES JR., and DR. R. G. GLADEN, Philadelphia.

Active immunization with the viruses of human influenza and swine influenza was carried out at a state colony for 800 feebleminded males. The purpose of the investigation was to determine: first, whether or not there was an increase in neutralizing substances in the serums of the vaccinated persons following vaccination and, second, whether or not there was a difference in the incidence of respiratory infections in the vaccinated group and the unvaccinated group. The viruses used were strain PR 8 human virus and strain 15 swine virus obtained through Dr. Francis and Dr. Shope.

Since the growth of one of the viruses, PR 8, in chick embryo mediums had not been constant, the vaccine used as a temporary expedient was a 10 per cent suspension of consolidated mouse lung passed through a Berkefeld V filter and tested for sterility and potency of virus. The vaccine was injected at weekly intervals in three doses of 0.5, 1, 1 cc., respectively, and produced no reaction other than slight local tenderness and erythema in a few cases. The colony was divided into three groups: those vaccinated with the virus of human influenza (110), those vaccinated with the virus of swine influenza (138) and those unvaccinated (550). Blood for neutralization tests was collected before vaccination and again two weeks following the third injection of vaccine.

Because the first neutralization tests showed that the undiluted serums of a large part of the colony neutralized both viruses, further tests were performed with dilutions up to 1:160. Both the group vaccinated with the virus of human influenza and the group vaccinated with the virus of swine influenza showed an increase in neutralizing substances to the homologous viruses and, to a lesser extent, to the heterologous viruses.

An epidemic of respiratory infections had been in progress for a short period before the vaccines were given. During the period of study following the vaccination such infections developed in 25 per cent of the colony. Ninety-two of this group had a temperature above 99.4 F. and were hospitalized; 110 were afebrile. Among the hospitalized patients, 4 were of the group vaccinated with the virus of human influenza; 19, of the group vaccinated with the virus of swine influenza, and 69, of the unvaccinated group (3.6, 13.7 and 12.5 per cent of the three groups, respectively). Among the afebrile patients, 18 were of the group vaccinated with the virus of human influenza; 21, of the group vaccinated with the virus of swine influenza, and 71 in the unvaccinated group (16.3, 14.3 and 12.9 per cent of these groups, respectively). On account of the character of the colony the data for the afebrile group were not entirely accurate. However, the records of the hospitalized patients were accurate and fairly complete.

There is no definite proof at present that the hospitalized patients had influenza. Certain evidence suggests that possibility: These cases were accompanied by clinical signs and symptoms simulating those of influenza; the white cell counts of the blood were relatively low in comparison with the elevation in temperature, and a few controls tested following respiratory illnesses showed an increase in neutralizing substances for the virus of human influenza.

DISCUSSION

DR. A. R. DOCHEZ, New York: I am much interested in this report. My associates and I are of the opinion that it represents the first positive result obtained in human beings by vaccination with the virus of an infection of the upper respiratory tract. It is of great interest that a number of infections of the upper respiratory tract in human beings are due to filtrable viruses and that the susceptibility of the upper respiratory tract to infection with these viruses is high.

My associates and I have never been able to make any studies of the neutralizing power of human serums of either infants or adults for the virus of the common

cold, the reasons being that we cannot infect small animals with the virus of the common cold and therefore are unable to titrate the protective powers of human serum. But in view of the fact that so many human serums, particularly, as one goes from young to older persons, protect animals adequately against infection with the influenza viruses, such as the virus of human influenza and the virus of swine influenza, it seems likely that if one were able to make the tests one would also find neutralizing substances in human blood for viruses of the lesser respiratory infections, such as ordinary grip and the common cold.

One of the confusing situations is that persons who seem to have a large amount of protective antibody are, nevertheless, highly susceptible to infection of the upper respiratory tract. This situation becomes apparent also in the study of ferrets that are immune to typical influenza virus. For several months following experimental infection the ferret is resistant to infection with the influenza virus, but after a certain length of time it again becomes susceptible to infection transmitted by intranasal inoculation. This susceptibility develops at the time when the ferret's blood contains neutralizing bodies for the virus in question. The animal at this time becomes susceptible again to the infection of the upper respiratory tract, and displays the nasal symptoms, but is not so likely to have infection of the deep respiratory tract. This is interesting in suggesting that even if one is not able to protect against the development of infection of the upper respiratory tract by means of vaccination it may be possible, as is indicated in these studies, to protect against the more severe types of infection, in which the virus passes beyond the upper respiratory mucous membranes and into the deep respiratory tract.

My associates and I have been vaccinating small groups of children with culture virus of the common cold and of influenza and using a carefully studied nonvaccinated group as control. Our results up to the present time, I am sorry to say, have been entirely negative. Of course, we are more particularly interested in the prevention of the common cold than in the prophylaxis of influenza, but the statistics collected by Kneeland to date (after a period of about two years) show practically the same incidence of infection of the upper respiratory tract in both the persons with and the persons without fever in the vaccinated group as well as in the unvaccinated group. Unfortunately, we were not able to study the development of protective substances in the serum of inoculated persons because the viruses with which we are working are not virulent for small animals. It is interesting that in the study reported there was no protective value in the vaccine of the virus of swine influenza; one would think that perhaps there might be some cross-effect.

Some years ago Kneeland made a study of the value of vaccinating young children with bacterial vaccines, using the types of pneumococcus and streptococcus that were prevalent in the institution. He vaccinated one group of children against these organisms and maintained another group as a control. He found that bacterial vaccine did not diminish the incidence of colds in the vaccinated group as compared with the unvaccinated group, but the amount of disability and hospitalization was less in the vaccinated group than in the unvaccinated group.

DR. C. F. MCKHANN, Boston: Is there any other discussion of this paper?

DR. J. D. TRASK, New Haven, Conn. I should like to inquire when the investigators started vaccinating the population in respect to the time of onset of the epidemic.

DR. ALICE CHENOWETH, Philadelphia: An epidemic was in progress at the time that we started the vaccinations and had been going on for about three weeks.

DR. J. STOKES JR., Philadelphia: It might be of interest that a few cultures from the throat were made for the secondary invaders, all of which revealed hemolytic streptococci. Influenza bacillus and pneumococcus were not found.

CHEMICAL CHANGES IN THE BLOOD SERUM IN PRIMARY PNEUMONIA OF CHILDREN; ACID-BASE BALANCE BEFORE AND AFTER CRISIS; INFLUENCE OF COMPLICATIONS. DR. H. COHEN and DR. P. R. MILLER, Brooklyn.

The paucity of data on the chemical changes occurring in the blood of children suffering from primary pneumonia led to the present study, which was carried out on 26 patients ranging in age from 6 months to 10 years. Particular emphasis was placed on the alterations of the acid-base equilibrium in the serum occurring before and after the crisis, as well as the changes accompanying complications. The study included variations found in the amount of total base, the value for chlorides, the total protein content, the amount of bicarbonate, the inorganic phosphorus content, the amount of nonprotein nitrogen and, in some instances, the cholesterol content.

The patients were divided into two groups, those exhibiting a definite crisis and those in whom the temperature dropped by lysis. Of the 13 patients who fell into the latter group, there was massive empyema in 6; in 1 there was a pulmonary abscess; in 2 resolution was delayed, and in the remainder there were no obvious complications. So far as was possible, the children were maintained on a more or less uniform diet to which no excess of sodium chloride was added. The amount of carbohydrate ingested ranged between 250 and 350 Gm. per day; the amount of protein, from 50 to 70 Gm., and the amount of fat, from 85 to 120 Gm. The intake of fluid varied between 1,000 and 1,500 cc. per day.

In the 13 cases in which there was a critical drop of temperature, the changes occurring during the fastigium were characterized by marked reduction in the amount of total base, accompanied by a similar and at times proportionate drop in the value of chlorides. A marked fall in the inorganic phosphorus content occurred regularly, together with a moderate degree of acidosis and some reduction of the total serum protein content. A variable concentration of undetermined acids was present. In general the return to normal occurred rapidly and was usually well established within a week after the crisis. However, the individual constituents varied in the rate of readjustment. The nonprotein nitrogen content, which was occasionally markedly elevated during the height of the illness, gradually returned to a normal level during convalescence. The diminished concentration of cholesterol present before the crisis rapidly returned to normal.

Profound changes in the acid-base equilibrium were found to be present in complicated cases of pneumonia. In empyema disturbances of the acid-base equilibrium were found to be as marked as those in the precritical period of primary pneumonia. When delayed resolution occurred the alterations in the chemical findings continued until the pathologic process had resolved.

DISCUSSION

DR. T. S. WILDER, Philadelphia: I should like to ask what the intake of sodium chloride was during the course of the pneumonia in these cases.

DR. A. A. WEECH, New York: May I add to Dr. Wilder's question by asking whether attempts were made to change the blood picture by administering sodium chloride?

DR. H. COHEN, Brooklyn: I mentioned in the introductory statement that no additional sodium chloride was given to any of the patients.

PHOSPHATASE ACTIVITY IN OSTEOGENESIS IMPERFECTA. DR. A. E. HANSEN, DR. I. MCQUARRIE and MISS MILDRED R. ZIEGLER, Minneapolis.

Few positive results have been obtained from the many attempts to study the nature of the underlying metabolic disturbances in osteogenesis imperfecta. Although the condition is regarded as a faulty development of the mesenchymal tissue, no reason has as yet been found to explain why the osseous tissue develops only to the point of nuclear bone formation.

The finding of an extremely low degree of activity of the enzyme phosphatase in the duodenal wall and in the periosteal and subperiosteal regions of the long bones in the case of one of our patients with osteogenesis imperfecta who died suddenly suggested the desirability of a more extensive study of the activity of the enzyme in this condition. During the past five years we have had the opportunity to study 7 patients who have come under our observation. The plasma phosphatase of specimens of blood during fasting in 4 of the patients indicated the degree of activity to be essentially normal. This finding has also been reported by other workers. While studies of the mineral balance indicate that these patients are capable of storing calcium and phosphorus under certain conditions, the amount stored was found by one of us to be but one-third that found in normal children under similar conditions. Antirachitic as well as all other forms of therapy have proved to be comparatively ineffective in this condition.

The present study deals with the effects of parathyroid extract and of viosterol in large doses on the plasma phosphatase activity in 4 cases of osteogenesis imperfecta. The findings in this study were correlated with the changes observed in the serum calcium content, the inorganic phosphorus content, the amount of total proteins and the nonprotein nitrogen content, as well as with the calcium and phosphorus balances. The following observations were made: Both the vitamin D and the parathyroid hormone caused a marked decrease in the activity of the plasma phosphatase. Both increased the serum calcium content significantly but produced little change in the values for the inorganic phosphorus, the nonprotein nitrogen and the total proteins of the serum. The retention of both calcium and of phosphorus was reduced conspicuously. The similarity of response to the two agents tends to favor the contention that vitamin D acts through the medium of the parathyroid glands. Our results indicate that the patient with osteogenesis imperfecta responds to these substances essentially like the normal subject. The observed correlation between the lowered activity of the blood phosphatase and the increased excretion of calcium and phosphorus suggests the possibility that factors which would increase the activity of the enzymes in the blood might at the same time have a beneficial effect on the retention of these elements.

DISCUSSION

Dr. W. W. Swanson, Chicago: I should like to ask Dr. Hansen whether the retention of sodium, potassium and chlorine was also determined in his studies of metabolism. My associates and I found in a similar investigation on an infant with osteogenesis imperfecta that not only the calcium and the phosphorus retention was disturbed but also the retention of potassium and of chlorine. Furthermore, we found that this infant, who was on cow's milk, retained an amount of calcium equal to that of an infant on breast milk.

Dr. A. E. Hansen, Minneapolis: We did not determine the values for sodium and potassium in the serum in any of our cases. Our studies of the mineral balance indicated that inadequate retentions of both calcium and phosphorus existed, but there were no abnormalities in any of the other elements studied. Our patients represented an older age group than those of Dr. Swanson. However, Dr. Harrison at New Haven found in a 10 month old infant with osteogenesis imperfecta a retention of calcium one-third that of 6 normal infants under exactly the same conditions of environment and diet.

Relationship Between Total and Free Cholesterol of the Blood Serum in Healthy and in Diseased Children. Dr. W. M. Sperry and Dr. J. D. Lyttle, New York.

In 60 healthy children between 10 months and 13 years old the percentage of free cholesterol in the total cholesterol content varied between a minimum of 25.3 and a maximum of 31. The range is practically the same as has been

found in healthy adults. About four fifths of 958 samples of serum from 302 children, most of whom were diseased, showed similar results. With few exceptions, values above 31 per cent of free cholesterol in the total cholesterol content were observed only in the presence of hepatic disease or infections (in most instances, acute infection). Conversely, with few exceptions, a normal proportion of free cholesterol in the total cholesterol content was not observed in the presence of hepatic disease or acute infection, although many values within the normal range were observed in the presence of mild, chronic and subsiding infections. The result leads to the conclusion that the percentage of free cholesterol in the total cholesterol content is a physiologic constant which has a wider range of usefulness in the detection of variation from the normal cholesterol metabolism than the absolute amounts present.

CHANGES IN THE VARIOUS FRACTIONS OF THE SERUM LIPIDS FOLLOWING ADMINISTRATION OF FATS WITH VARIOUS DEGREES OF UNSATURATION AND DIFFERENT MOLECULAR WEIGHTS. DR. A. E. HANSEN, Minneapolis.

The development by Wilson and me of a microgravimetric method for the isolation of the saponifiable fraction of the serum lipids has stimulated further investigation of the fatty acids in the various fractions of the blood. By this method it is possible to obtain such qualitative values of the fatty acids as milliequivalents, the saponification number, the average molecular weight, the iodine number, the average number of double bonds per molecules of fatty acids and also the total weight of the saponifiable and the unsaponifiable fractions. Preliminary studies by Wilson and me revealed that when dogs were fed on diets containing fats of widely different molecular weights the average molecular weight of the fatty acids of the serum tended to remain constant. The iodine numbers of the fatty acids on specimens of blood during fasting, however, were greatly affected under these conditions, corresponding to the difference in the degree of unsaturation of the dietary fats. Valuable information might be obtained concerning the underlying nature of certain clinical disorders involving the lipid metabolism if more studies were extended to include information concerning the character of the phospholipid fatty acids of the blood. This we are attempting to carry out in our laboratory under a variety of conditions. The lipid phosphorus present in the acetone-insoluble fraction of the serum lipids is between 50 and 60 per cent of the total lipid phosphorus content. In the present study an attempt has been made to isolate the fatty acids present in the acetone-insoluble fraction (phospholipid), using a modification of Bloor's procedure and the technic developed by Wilson and me for determining the molecular weights and quantitative values of fatty acids. The preliminary findings indicate that the average molecular weight of these fatty acids is significantly higher than the average molecular weight of the total fatty acids. This might well be accounted for in part by the presence of the 20 carbon-atom acid, arachidonic acid, which we have found in appreciable amounts in the serum of patients with eczema. Our results might also be regarded as confirmatory evidence of the occurrence of sphingomyelin in this fraction, because the latter contains lignoceric acid with its 24 carbon atoms.

DISCUSSION

DR. W. M. SPERRY, New York: It seemed to me in a rough calculation from the last slide that the average molecular weights of the fatty acids were rather high, in comparison with the iodine numbers, to be accounted for by arachidonic acid. I wonder if any calculations were made as to whether these two factors can be correlated. Is it possible that acids of the tetra-cosanic series were present? Such acids, not being saturated or perhaps having one bond, would of course account for a high molecular weight and a low iodine number. The iodine numbers appeared low in comparison with those which have usually been reported for phospholipid fatty acids from other sources.

DR. A. E. HANSEN, Minneapolis: The only comparable figures that I have been able to find on the isolated fatty acids of phospholipids are those of Bloor. He used large samples of blood from the sheep, the dog and the ox, and his figures are similar to ours.

If lignoceric acid or any of the longer chain saturated fatty acids are present in the blood to any great extent, this would tend to diminish the iodine number more than arachidonic acid would tend to increase it. We hope to gain more information on the nature of these fatty acids of the blood during the course of our investigations.

BOROTARTRATE IN THE TREATMENT OF EPILEPSY IN CHILDHOOD. DR. L. KAJDI, Baltimore.

Borax has been used for more than a hundred years as a remedy for convulsions. Growers reported that 60 per cent of his patients improved and 10 per cent became free from attacks with this treatment. The disadvantage of borax lies in the fact that it has to be used in large doses; it has a nauseating taste, and it frequently causes indigestion and annoying cutaneous manifestations. These were eliminated when Pierre Marie introduced borotartrate. In large doses this may cause a depressive, apathetic or confused state which promptly clears up on withdrawal of the drug. It is a diuretic, lowers the urinary p_H, increases the globulin fraction in the serum, decreases the swelling capacity of colloids, decreases the amount of serum potassium and possibly prevents spasm of the blood vessels; all these factors were claimed to inhibit the occurrence of attacks. It is not a narcotic drug. It is seldom effective alone and it is recommended for use in combination with other sedatives. I have confirmed the observations of Bovet and of Carrier that it frequently counteracts the depressive action of sedative drugs.

In the last three and a half years it was used in 75 of the 200 patients with epilepsy followed by me. In 6 cases borotartrate alone was used; in 1 patient the attacks ceased, the other patients were not benefited. Among 3 cases, in which a ketogenic diet failed to control the attacks, even when reenforced with sedatives, the addition of borotartrate stopped the attacks in 1, and in the other 2 it effected moderate improvement.

Among 54 patients in whom the previous sedative therapy failed, the attacks ceased in 9; 9 were much improved; 7 were only moderately benefited, and in 29 the treatment failed. (Patients were considered to be much benefited if only occasional aura-like attacks occurred and moderately so if attacks were reduced to at least one fourth of the original number.)

Seventeen patients received the borotartrate therapy combined with other drugs without previous trial of sedatives. Eight became free from attacks; 2 were much benefited and 3 only moderately benefited, and in 4 the disease was not influenced by this treatment.

I feel that the treatment with borotartrate combined with other sedatives promises to be a valuable addition to the symptomatic treatment of epilepsy.

DISCUSSION

DR. E. M. BRIDGE, Baltimore: If one is accustomed to dealing with patients who are treated with something as specific as insulin the results which Dr. Kajdi has presented do not perhaps seem so significant as they do if one is accustomed to dealing with a disease with a multitude of contributing factors such as epilepsy.

Actually, the percentage of results which he has reported are practically as good as can be obtained with phenobarbital, bromide or the ketogenic diet alone, so that in spite of 44 per cent of failures and only from 20 or 25 per cent of good results, this treatment is one more valuable addition to the therapeutic armamentarium in cases of epilepsy.

QUESTION: Can Dr. Kajdi tell the members the dosage of the drugs?

DR. L. KAJDI, Baltimore: I used the drug in doses of 15 or 10 grains (0.9 or 0.6 Gm.) two or three times a day, depending on how much sedative I had to use. The main importance of this drug is that it is not sedative and even counteracts the sedative action of the other drugs, so that it is possible to use the phenobarbital or bromide in larger doses than without borotartrate. The use of borotartrate is justified in the case of patients who would not be benefited otherwise. The ketogenic diet can be used only for a child with intelligence whose parents are relatively well-to-do. Only those persons who have tried a ketogenic diet know what the child has to suffer when he has to eat it for months.

Book Reviews

The Adrenals. By Arthur Grollman, Ph.D., M.D. Price, $5. Pp. 410, with 17 illustrations. Baltimore: Williams & Wilkins Company, 1936.

In this volume Grollman, a well known investigator in the field of the adrenal glands, has given a complete account of the development of the knowledge of these interesting and important glands: the brilliant researches that led to the identification of their two hormones and the final synthesis of epinephrine and the no less brilliant but so far futile endeavors to discover the real functions in the body economy of these two potent substances.

After a brief historical résumé the subject matter is presented in four parts: (1) anatomic considerations, (2) the medulla, (3) the cortex and (4) clinical considerations.

Part 1 gives a full statement of the gross and microscopic anatomic features of the glands themselves and the accessory adrenal tissues and derives especial interest from the author's discussion of his ideas regarding the "androgenic" tissue, the clinical implications of which he considers again in part 4.

Part 2 begins with the story of the discovery and final synthesis of epinephrine and goes on to a detailed statement of methods of physiologic and pharmacologic study of the medulla and epinephrine and the theories and established facts regarding the hormone's action.

Part 3, while devoted to the cortex, actually takes up the whole question of adrenal function and the complicated literature on adrenalectomized animals. As no definite effects from deprivation of epinephrine have ever been proved, these studies have resolved themselves into investigations of cortical insufficiency and its relations to the various systems of the body, to the blood chemistry and the metabolism and to surgical shock and other conditions; a thorough discussion is given. The story of adrenal cortex extract and its chemistry and pharmacology is brought up to date.

In part 4, on clinical considerations, Grollman discusses Addison's disease, tumors of the adrenal glands and other conditions and gives considerable space to the androgenic tissue and the "androgenital syndrome," a favorite subject with him. He takes up the possible relationship of this tissue to virilism, hermaphroditism, Cushing's syndrome and other disorders.

The book is complete and contains a wealth of scientific information. It is not a popular treatise. The long history of complicated investigation is presented in a way that seems at times unnecessarily obscure and confusing and is marred in places by annoying mistakes due to careless proof-reading. Abundant material is, however, here at hand for one who wishes to be informed on the subject of the adrenal glands and the many controversies which it has aroused.

Your Baby and Child. By M. C. Overton, M.D. Cloth. Price, $2. Pp. 224, with 2 illustrations. Lubbock, Texas: Your Baby and Child Publishing Co., 1936.

In this book Overton has developed a rather unique plan to inform the mother of such facts as he thinks it necessary for her to know. There are no chapters, but he has selected one hundred and thirty-five subjects for discussion. He does not use the silly question and answer method of presentation but gives a lucid brief exposition of essential topics varying from breast feeding (covered in six pages) to cradle cap (discussed in a quarter of a page). The subjects are especially well chosen, and the book is well written. Overton has made no effort to impress the mother with his unbounded wisdom on all matters but keeps to his

subjects in a logical way. Debatable points are stated as such, and no dogmatic rules are laid down to the detriment of other schools of thought. This is especially true in the discussion of feeding and the vitamins. A new "high" is reached in that there is no advertising of commercial products. Every book for the laity that the reviewer has seen in the last few years has contained numerous references to specifically named commercial products. Only one such product is mentioned in this book. The physician need not be afraid to recommend this book to his patients.

A Study of Masturbation and the Psychosexual Life. By Dr. John F. W. Meagher. Third edition. Price, $2. Pp. 141. Baltimore: William Wood & Company, 1936.

This, the third edition, was reedited and revised by Dr. Smith Ely Jelliffe. The general characteristics of the original editions are retained.

Emphasis is placed on the psychologic nature of sex, its characteristics at various periods of life, its influence on personality development and the importance of the right attitude toward sex on the part of parents, teachers, physicians, clergymen, etc.

The rôle of masturbation in sex development is described in detail. Masturbation is pictured as normal in infancy, common in adolescence and abnormal in adult life. Emphasis is placed on the psychologic aspects of masturbation, there being no harmful physical effects. The final chapters deal with the causes and treatment of excessive or abnormal masturbation.

The book is clearly written and instructive. The general point of view and attitude taken by the author are especially valuable.

Fifth National Medical Congress, Acts and Works, Rosario, Argentina. Pp. 519, with 80 illustrations. Rosario: Talleres Graficos Pomponio, 1934.

This book is an official record of the proceedings of the Fifth National Medical Congress of Argentina. It contains the scientific papers presented. "The Epidemiology of Amebiasis," by Salvador Mazza, is a good general review of the subject. Dr. Marino R. Castex and Dr. Daniel Greenway presented a paper covering the parasitology and clinical findings in 2,700 cases of intestinal amebiasis. Dr. David Staffieri read a complete and excellent paper on the extra-intestinal lesions and locations of the ameba, discussing in detail the symptoms, clinical course, pathologic features and treatment of all the varieties of amebiasis other than intestinal. A paper entitled "Surgery and Amebiasis" was read by Dr. R. A. Marotta. Other papers presented include "Surgical Possibilities in the Treatment of Spastic Paralysis," by Dr. Manuel B. Ansart; "Filtrable Virus of Psittacosis in Particular," by Dr. Thomas, and "The Respiratory Insufficiencies and the Scientific Basis for Pulmonary Collapse Therapy," by Dr. L. Brauer.

Die Bierhefe als Heil-, Nähr-und Futtermittel. By Dr. Julius Schülein. **Band XXXV, Technischen Fortschrittsberichte: Fortschritte der Chem. Technologie in Einzeldarstellungen,** edited by B. Rassow. Price, paper, 9 marks; bound, 10 marks. Pp. 200, with 21 illustrations. Dresden: Theodore Steinkopff, 1935.

This book is intended as a review of recent work on brewers' yeast (and the chemistry of this substance) as a therapeutic agent, as a source of vitamins and as a feed in animal husbandry. The book is primarily intended for the technologist and research worker in the brewers' yeast industry and contains little of interest to the physician. The aim and intent of the work are well accomplished, and, while the book is small, more than four hundred references to the recent literature on the subject are cited.

The Baby and Growing Child. By Louis Fischer, M.D. Price, $1.50. Pp. 260, with 22 plates and figures. New York: Funk & Wagnalls Company, 1936.

The first part of this book treats of the hygiene of the infant; part two discusses feeding; part three deals with nervous manifestations; part four is on contagious diseases, and the final chapter is devoted to miscellaneous recipes. The work is well written and might be as useful as the usual book of this type for the mother, but the reviewer fails to see the point of specifying "Carnation milk (irradiated)" and "Viosterol made by Mead, Johnson & Co." or of including plates, by Courtesy of the Davol Rubber Co., on short nipples.

Rapport sur le Service des Enfants Assistés du Département de la Seine, 1934. Part II. By Louis Mowier. Pp. 69, with 14 tables. Paris: Administration Générale de l'Assistance Publique à Paris, 1936.

This is the second part of the report of the Director General of the Administration of Public Assistance of the Department of the Seine and consists entirely of the financial statement. The first part, on the administration, has already been reviewed.

Directory of Pediatric Societies

INTERNATIONAL

International Association of Preventive Pediatrics

President: Professor G. Scheltema, 6a Heereplein, Groningen, The Netherlands.
Secretary: Dr. Daniel Oltramare, 15 Rue Lévrier, Geneva, Switzerland.

FOREIGN

British Paediatric Association

President: Dr. Leonard Findlay, 14 Wimpole St., London, W. 1.
Secretary: Dr. Arthur G. Maitland Jones, 31A Weymouth St., London, W. 1.

Royal Society of Medicine, Section for the Study of Disease in Children

President: Sir Lancelot Barrington-Ward, 85 Harley St., London, W. 1.
Secretary: Dr. K. H. Tallerman, 122 Harley St., London, W. 1.
Place: 1 Wimpole St., London. Time: Fourth Friday of each month, 4:30 p. m.

Paediatrický Spolok na Slovensku

President: Dr. A. J. Chura, Lazaretská 6, Bratislava, Czechoslovakia.
Secretary: Dr. S. Limbacher, Dlhá 2, Bratislava, Czechoslovakia.
Place: Pediatric Clinic, University, Bratislava. Time: Six times a year.

Sociedad Cubana de Pediatría

President: Prof. Félix Hurtado Galtés, Carlos III, 7, Havana.
Secretary: Dr. Carlos Hernández Miyares, San Lazaro 370, Havana.
Place: Cátedra de Clínica Infantil, Hospital Mercedes, Havana. Time: Third Thursday of every month.

NATIONAL

American Medical Association, Scientific Assembly, Section on Diseases of Children

Chairman: Dr. Ralph M. Tyson, 255 S. 17th St., Philadelphia.
Secretary: Dr. Albert D. Kaiser, 16 N. Goodman St., Rochester, N. Y.
Place: Atlantic City, N. J. Time: June 7-11, 1937.

American Academy of Pediatrics

President: Dr. Laurence R. DeBuys, 1417 Delachaise St., New Orleans, La.
Secretary: Dr. C. G. Grulee, 636 Church St., Evanston, Ill.
Place: Waldorf-Astoria Hotel, New York: Time: June 3, 4 and 5, 1937.
Region I. Place: Belvedere Hotel, Baltimore. Time: Nov. 16 and 17, 1936.
Region II. Place: Belvedere Hotel, Baltimore. Time: Nov. 16 and 17, 1936.
Region III. Place: Cincinnati. Time: Nov. 20 and 21, 1936.
Region IV. Place: San Francisco. Time: Oct. 22-24, 1936.

American Hospital Association, Children's Hospital Section

President: Mr. Robert Witham, Children's Hospital, Denver.
Secretary: Miss Agnes O'Roke, Kosair Crippled Children's Hospital, Louisville, Ky.

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* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

American Pediatric Society

President: Dr. Fritz B. Talbot, 270 Commonwealth Ave., Boston.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid St., St. Louis.

Canadian Society for the Study of Diseases of Children

President: Dr. A. P. Hart, 1844 Bloor St., W., Toronto, Ont.
Secretary-Treasurer: Dr. Pearl Summerfeldt, Hospital for Sick Children, Toronto, Ont.

Society for Pediatric Research

President: Dr. Francis Scott Smyth, University of California Medical School, San Francisco.
Secretary: Dr. A. A. Weech, 3975 Broadway, New York.

SECTIONAL

North Pacific Pediatric Society

President: Dr. L. Howard Smith, 1020 S. W. Taylor St., Portland, Ore.
Secretary: Dr. Morris Bridgeman, Children's Clinic, Portland, Ore.

Southern Medical Association, Section on Pediatrics

Chairman: Dr. Madison Hines Roberts, 104 Ponce de Leon Ave., N. E., Atlanta, Ga.
Secretary: Dr. Hughes Kennedy Jr., Highland Plaza Apts., Birmingham, Ala.

STATE

Alabama Pediatric Society

President: Dr. J. W. Britton, 931 Noble St., Anniston.
Secretary-Treasurer: Dr. Wallace Clyde, Employees' Hospital, Fairfield.

Arkansas State Pediatric Association

Chairman: Dr. A. C. Kirby, 701 Main St., Little Rock.
Secretary: Dr. Madeline M. Melson, 909 Main St., Little Rock.

California State Medical Society, Section on Pediatrics

Chairman: Dr. Edward B. Shaw, 384 Post St., San Francisco.
Secretary: Dr. E. Earl Moody, 3780 Wilshire Blvd., Los Angeles.

Florida State Pediatric Society

President: Dr. Luther W. Holloway, 117 W. Duval St., Jacksonville.
Secretary: Dr. Warren W. Quillian, 227 Avenue Aragon, Miami.
Place: Concurrent with state association meeting at time of convention.

Georgia Pediatric Society

President: Dr. Mercer Blanchard, 1301 Broadway, Columbus.
Secretary-Treasurer: Dr. Don F. Cathcart, 478 Peachtree St., N. E., Atlanta.
Place: Atlanta. Time: December 1936.

Indiana State Pediatric Society

President: Dr. Milo K. Miller, 122 N. Lafayette Blvd., South Bend.
Secretary-Treasurer: Dr. Mathew Winters, 23 E. Ohio St., Indianapolis.
Time: Two meetings a year.

LOUISIANA STATE PEDIATRIC SOCIETY

President: Dr. Charles James Bloom, 3439 Prytania St., New Orleans.
Secretary-Treasurer: Dr. J. A. Crawford, 834 Ryan St., Lake Charles.

MEDICAL SOCIETY OF STATE OF NEW YORK, SECTION ON PEDIATRICS

Chairman: Dr. George M. Retan, 459 James St., Syracuse.
Secretary: Dr. John D. Craig, 33 E. 61st St., New York.

MICHIGAN STATE MEDICAL SOCIETY, PEDIATRIC SECTION

Chairman: Dr. Edgar E. Martmer, 749 David Whitney Bldg., Detroit.
Secretary: Dr. C. R. Dengler, 131 W. Michigan Ave., Jackson.

MISSISSIPPI STATE PEDIATRIC SOCIETY

President: Dr. Harvey F. Garrison, 319 E. Capitol Pl., Jackson.
Secretary-Treasurer: Dr. Guy C. Jarratt, 920 Crawford St., Vicksburg.
Place: To be designated by Society. Time: Yearly.

NEBRASKA PEDIATRIC SOCIETY

President: Dr. J. A. Henske, 1614 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. J. H. Murphy, 915 Medical Arts Bldg., Omaha.
Place: As announced by committee. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

NORTH CAROLINA PEDIATRIC SOCIETY

President: Dr. Leroy J. Butler, 405 N. Spring St., Winston-Salem.
Secretary: Dr. C. A. Street, 405 N. Spring St., Winston-Salem.

OKLAHOMA STATE PEDIATRIC SOCIETY

President: Dr. Julian Feild, 610 S. Monroe St., Enid.
Secretary: Dr. B. H. Nicholson, 301 N. W. Twelfth St., Oklahoma City.

PENNSYLVANIA MEDICAL SOCIETY, PEDIATRIC SECTION

Chairman: Dr. Joseph Stokes, Children's Hospital, Philadelphia.
Secretary: Dr. Theodore O. Elterich, 310 Medical Arts Bldg., Pittsburgh.

SOUTH CAROLINA PEDIATRIC SOCIETY

President: Dr. Leland B. Salters, 317 S. Warley St., Florence.
Secretary-Treasurer: Dr. D. Lesesne Smith Jr., 187 Oakland Ave., Spartanburg.

TENNESSEE STATE PEDIATRIC SOCIETY

President: Dr. Joe T. Smith, 702 Medical Arts Bldg., Knoxville.
Secretary: Dr. Kinsey M. Buck, 1193 Madison Ave., Memphis.

TEXAS PEDIATRIC SOCIETY

President: Dr. George B. Cornick, 507½ E. Houston St., San Antonio.
Secretary-Treasurer: Dr. F. H. Lancaster, 1507 Medical Arts Bldg., Houston.
Place: Houston. Time: Fall, 1936.

VIRGINIA PEDIATRIC SOCIETY

President: Dr. Basil B. Jones, 1028 W. Franklin St., Richmond.
Secretary: Dr. W. A. McGee, 616 W. Grace St., Richmond.

WEST VIRGINIA STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

President: Dr. John T. Thornton, 58, 16th St., Wheeling.
Secretary: Dr. Claude L. Holland, 400 Locust Ave., Fairmont.

LOCAL

Academy of Medicine of Cleveland, Pediatric Section

Chairman: Dr. J. D. Pilcher, City Hospital, Cleveland.
Secretary: Dr. William M. Champion, 2323 Prospect Ave., Cleveland.
Place: Cleveland Medical Library Bldg. Time: October, December, February and April.

Academy of Medicine, Toronto, Section of Pediatrics

President: Dr. T. B. Verner, 170 St. George St., Toronto.
Secretary: Dr. D. V. Hutton, 170 St. George St., Toronto.

Bronx Pediatric Society

President: Dr. Harry D. Pasachoff, 1560 Grand Concourse, New York.
Secretary: Dr. Samuel Tripler, 1555 Grand Concourse New York.
Place: Concourse Plaza Hotel, 161st St. and Grand Concourse. Time: Every second Wednesday of each month, except June, July, August and September.

Brooklyn Academy of Pediatrics

President: Dr. Thurman B. Givan, 115 Remson St., Brooklyn.
Secretary: Dr. John A. Monfort, 861 Carroll St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Fourth Wednesday of each month, except May, June, July, August and September.

Central New York Pediatric Club

President: Dr. Frank Vasder Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Third Thursday of April and September.

Chicago Pediatric Society

President: Dr. A. Levinson, 30 N. Michigan Ave., Chicago.
Secretary: Dr. James H. Wallace, 715 Lake St., Oak Park, Ill.
Place: Children's Memorial Hospital, 710 Fullerton Ave. Time: Third Tuesday of each month.

Dallas Pediatric Society

President: Dr. I. T. Nesbitt, 1719 Pacific Ave., Dallas, Texas.
Secretary: Dr. John E. Ashby, 614 Medical Arts Bldg., Dallas, Texas.
Place: Bradford Memorial Hospital. Time: 1 p. m., first and third Saturdays of each month.

Detroit Pediatric Society

President: Dr. Edward A. Wishropp, 10 Peterboro St., Detroit.
Secretary: Dr. W. J. Scott, 5140 Second Ave., Detroit.
Place: Wayne County Medical Society. Time: 8:30 p. m., first Wednesday of each month from October to June, inclusive.

Fulton County Medical Society, Pediatric Section (Atlanta, Ga.)

Chairman: Dr. Joseph Yampolsky, 478 Peachtree St., Atlanta.
Secretary: Dr. T. I. Willingham, 384 Peachtree St., Atlanta.
Place: Academy of Medicine, 38 Prescott St., N. E. Time: Second Thursday of each month from October to April, 8 p. m.

Hezekiah Beardsley Pediatric Club of Connecticut

President: Dr. H. W. Brayton, 179 Allyn St., Hartford.
Secretary: Dr. Ernest Caulfield, 683 Asylum Ave., Hartford.

Houston Pediatric Society

President: Dr. E. O. Fitch, 3717 Main St., Houston, Texas.
Secretary-Treasurer: Dr. Fred Ames, Medical Arts Bldg., Houston, Texas.
Place: Houston Club. Time: Third Monday of each month.

Intermountain Pediatric Society

President: Dr. Eugene Smith, 385 Twenty-Fourth St., Ogden, Utah.
Secretary-Treasurer: Dr. W. C. Cheney, 837 Boston Bldg., Salt Lake City, Utah.
Place: Salt Lake City, General Hospital. Time: First Thursday of each month, 8 p. m.

Kansas City (Missouri) Pediatric Society

President: Dr. Harry M. Gilkey, 1103 Grand Ave., Kansas City.
Secretary: Dr. S. A. Stadler, 6133 Brookside Blvd., Kansas City.
Place: Kansas City General Hospital. Time: On call.

Los Angeles County Medical Association, Pediatric Section

President: Dr. George P. Laton, 1136 W. 6th St.
Secretary-Treasurer: Dr. Edwin F. Patton, 3875 Wilshire Blvd., Los Angeles.
Place: Los Angeles County Medical Headquarters, 1925 Wilshire Blvd.
Time: Second Monday of February, April, June, October and December.

Medical Society of the County of Kings and the Academy of Medicine of Brooklyn, Pediatric Section

President: Dr. Harry Apfel, 988 Park Pl., Brooklyn.
Secretary: Dr. Max Palinsky, 1270, 45th St., Brooklyn.
Place: 1313 Bedford Ave., Brooklyn. Time: Third Wednesday of each month, October to May.

Medical Society of the County of Queens, Inc., Section on Pediatrics

Chairman: Dr. W. C. A. Steffen, 42 Union St., Flushing, N. Y.
Secretary-Treasurer: Dr. Edith A. Mittell, 144, 38th Ave., Flushing, N. Y.
Place: Queens County Medical Bldg., Forest Hills, N. Y. Time: Third Monday of October, January, March and May.

Memphis Pediatric Society

President: Dr. W. D. Mims, 1042 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. W. R. Graves, 1193 Madison Ave., Memphis, Tenn.
Place: Memphis General Hospital. Time: Second Tuesday of each month, except June, July and August, 8 p. m.

Milwaukee Pediatric Society

President: Dr. J. Gurney Taylor, 324 E. Wisconsin St., Milwaukee.
Secretary: Dr. H. B. Miner, 425 E. Wisconsin Ave., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

New England Pediatric Society

President: Dr. Paul Emerson, 319 Longwood Ave., Boston.
Secretary-Treasurer: Dr. Henry E. Gallup, 66 Commonwealth Ave., Boston.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. Béla Schick, 17 E. 84th St., New York.
Secretary: Dr. Alexander T. Martin, 107 E. 85th St., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

Northwestern Pediatric Society

President: Dr. A. V. Stoesser, University Hospital, Minneapolis.
Secretary: Dr. Roger L. J. Kennedy, Mayo Clinic, Rochester, Minn.
Place: Minneapolis, St. Paul, Duluth and Rochester. Time: January, April, July and October.

Philadelphia Pediatric Society

President: Dr. H. H. Perlman, 1904 N. Franklin St., Philadelphia.
Secretary: Dr. James E. Bowman, 4091 Comly St., Philadelphia.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to June, inclusive.

Pittsburgh Pediatric Society

President: Dr. James LeRoy Foster, Highland Bldg., Pittsburgh.
Secretary-Treasurer: Dr. E. R. McClusky, 3200 Fifth Ave., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate months from October to April, inclusive.

Richmond Pediatric Society

President: Dr. W. E. Chapin, 1001 E. Clay St., Richmond, Va.
Secretary-Treasurer: Dr. Emily Gardner, 1100 W. Franklin St., Richmond, Va.
Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: First Thursday of each month (except July, August and September).

Rochester Pediatric Society

President: Dr. F. W. Bush, 29 N. Goodman St., Rochester, N. Y.
Secretary: Dr. David Wolin, 16 N. Goodman St., Rochester, N. Y.
Place: Arranged by program committee. Time: Second Friday of each month.

Rocky Mountain Pediatric Society

President: Dr. Ralph Verploeg, 1850 Gilpin St., Denver.
Secretary: Dr. Max M. Ginsburg, Metropolitan Bldg., Denver.
Place: Children's Hospital, Denver. Time: First Saturday of each month from September to May, inclusive, 2:30 p. m.

St. Louis Pediatric Society

President: Dr. J. V. Cooke, St. Louis Children's Hospital, St. Louis.
Secretary-Treasurer: Dr. Katherine Bain, Beaumont Bldg., St. Louis.
Place: St. Louis Medical Society. Time: Third Friday of every month.

Seattle Pediatric Society

President: Dr. Arthur E. Wade, 1215, 4th Ave., Seattle.
Secretary: Dr. Walter B. Seelye, Cobb Bldg., Seattle.
Place: College Club. Time: Third Friday of each month, 6:30 p. m.

Southwestern Pediatric Society

President: Dr. Victor E. Stork, 1136 W. Sixth St., Los Angeles.
Secretary: Dr. Howard R. Cooder, 3875 Wilshire Blvd., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

University of Michigan Pediatric and Infectious Disease Society

President: Dr. Samuel Levin, 2501 W. Grand Blvd., Detroit.
Secretary: Dr. D. Murray Cowie, University of Michigan, Ann Arbor, Mich.

Westchester County Medical Society, Pediatric Section (New York)

President: Dr. Louis V. Waldron, 149 N. Broadway, Yonkers, N. Y.
Secretary-Treasurer: Dr. Fairfax Hall, 421 Huguenot St., New Rochelle, N. Y.
Place: Grasslands Hospital. Time: Third Thursday, Oct., Dec., Feb. and April